Remarks

Upon entry of the foregoing amendments, claims 16-18, 22-25, 27 and 33 are under consideration. Applicants have amended claims 16, 22, 25, 27. Specifically, Applicants have amended these claims to now recite the further limitation "wherein said polypeptide may be used in a diagnostic assay." Basis for this amendment can be found in the Specification as originally filed, and in particular at page 36, lines 27-30; page 28, lines 15-18; page 30, lines 27-35; and page 38, lines 25-30. Further, Applicants have canceled claims 19-21, 26, 28-32, and 34, in order to expedite prosecution and allowance of present application. Applicant reserves its right to prosecute the subject matter in later application.

Applicants assert that the present amendments add no new matter.

THE §101 REJECTION

The Examiner has rejected claims 16-34 under 35 U.S.C. §101, alleging that the claimed Invention is not supported by either a substantial asserted utility or a well established utility, as the claimed polypeptides are directed to "an orphan neuro-growth factor." Specifically, the Examiner has alleged that the claimed polypeptides do not have substantial utility because the utility is based on homology, and a skilled artisan would need to prepare, isolate, and analyze the protein in order to determine its function and use.

Applicants disagree. Applicants respectfully submit that the rejection is contrary to both the law and the United States Patent Office's own examination guidelines for the following reasons.

1) Subsequent Analysis of Zneu1 Indicates Utility

Utility for Applicant's use of Zneu1 is of a nature that one of skill in the art will immediately appreciate. The application of these standards to biotechnology inventions is discussed in the January 5, 2001 Utility Examination Guidelines, which state:

> An invention has a well-established utility if a person of ordinary skill would immediately appreciate why the invention is useful based on the characteristics of the invention (e.g., properties...), and the utility is specific, substantial, and credible...

See e.g. Utility Examination Guidelines, 66 F.R. 4 at pg. 1098, §II.B.1(c)(1). Moreover, "[a] patent examiner must accept a utility asserted by an applicant unless the Office has sound scientific reasoning to rebut the assertion." *Id.*

Applicants have completed subsequent RT-PCR analyses of Zneu1 expression using cDNA tumor panels and matched cDNA pairs from tumor and normal tissues. The study indicates that Zneu1 is up-regulated in tumor tissues and is not up-regulated in normal tissues. Therefore, Zneu1 would be suitable for use as a diagnostic cancer marker. Furthermore, the Specification specifically describes Zneu1's use as a diagnostic cancer marker:

> The binding proteins can also be used for diagnostic assays for determining circulating levels of polypeptides; for detecting or quantitating soluble polypeptides as marker of underlying pathology or disease.

See e.g. Specification at page 36, lines 27-30; *see also* page 28, lines 15-18; page 30, lines 27-35; and page 38, lines 25-30.

Accordingly, Applicants further assert that, due to this specific and substantial utility, Zneu1 would be immediately recognized by one of skill in the art as having a substantial asserted utility and a well-established utility.

2) Court Precedent Points To Utility by Homology For Zneu1

Courts have routinely accepted that an assertion of a specific pharmacological activity for a newly discovered molecule (i.e. Zneu1) may, in some limited circumstances, be justified through homology:

> ...a particular pharmacological activity identified with prior art compounds may have probative value as to the fact that the compound of the count possesses this particular pharmacological activity where there is a structural similarity between the prior art compounds and the compound of the count.

Cross v. Iizuka, 753 F.2d 1040, 1048, 224 USPQ 739 (Fed. Cir. 1985) citing *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1385-87, 181 USPQ (BNA) 453 (1974) (where the Board of Patent Interferences was looking for utility to establish a reduction to practice) (for Examiner's

convenience, Applicants have enclosed copies of all cases cited herein). Furthermore, the Courts have also recognized that pharmacological activity is sufficient to establish utility. *Cross*, 753 F.2d at 1047; *Nelson v. Bowler*, 626F.2d 853, 206 USPQ 881 (CCPA 1980); *In re Jolles*, 628 F.2d 1322, 206 USPQ 885 (CCPA 1980). Thus, as homology may show pharmacological activity and as pharmacological activity may show utility, homology may show utility in some limited circumstances. Applicants assert that Zneu1 has utility due to its homology with the well-characterized endothelial-specific gene Notch 4. *See e.g.* Specification at pages 24-27.

However, Applicants acknowledge that there are two limitations on the use of homology to establish pharmacological activity, as described above. First, reduction to practice must require no more than ordinary skill in the art:

> That which determines if the mental formulation of the invention rises to the level of conception is whether or not the inventor has also conceived the means of putting that formulation in the hands of the public where no more than routine skill would be required to do so.

Rey-Bellet, 493 F.2d 1380. Second, when using homology as a basis for utility, the Application must not claim more than a single use for the Invention. The concern is that the scope of the grant will be unduly large; this is why *Brenner* states, "...a patent is not a hunting license." *Brenner v. Manson*, 383 U.S. 519, 535, 536, 148 USPQ 689 (1966). *Rey-Bellet* harmonizes with the *Brenner* Court's concern, regarding scope of claimed material, when it instructs that homology can only establish utility if a single use is claimed. *Rey-Bellet*, 493 F.2d 1380.

Accordingly, Applicants assert that one of ordinary skill in the art could *easily* reduce to practice the present Invention. Reduction to practice would merely require one skilled in the art to create an industrially acceptable promoter and terminator and the subsequent up-scaling of production – both of which will take no more than regular skill in the art to accomplish. In this way, Zneu1 can be easily reduced to practice for use as a diagnostic cancer marker. Second, Applicants have claimed no more than a single intended use for the polypeptide (i.e. a diagnostic cancer marker); this is corroborated by Applicant's subsequent studies and can be further corroborated by an oath from the Inventor. Applicants would note that testimony of the Inventor was sufficient in *Rey-Bellet* to show a singular intended use. *Rey-Bellet*, 493 F.2d 1380.

As both limitations are met, Applicants state that Zneu1's homology to Notch 4 is a strong indication of a specific pharmacological activity (i.e. that of Notch 4). As pharmacological activity is sufficient to establish utility; therefore, Applicants further assert that Zneu1 has utility; and as such, Applicants state that Zneu1 would be recognized by one of skill in the art as having a substantial asserted utility and a well-established utility. Consequently, Applicants request that the Examiner withdraw the present rejection under 35 U.S.C. §101.

THE §112, FIRST PARAGRAPH REJECTION

The Examiner has rejected claims 18, 21, 24, and 30 under 35 U.S.C. § 112 alleging that the term "immunoglobulin domain" is new matter because the Specification does not disclose the claimed Invention.

Applicants traverse. "Immunoglobulin domain" is disclosed in the Specification at page 22, lines 38-40 and at page 23, lines 1-2. Accordingly, Applicants request withdrawal of the present rejection.

The Examiner has also rejected claims 28-34 under 35 U.S.C. § 112 alleging that the specific residues of SEQ ID NO: 3 are new matter because the Specification does not disclose the claimed Invention.

Applicants traverse. Applicants would like to clarify that claim 33 is dependent upon claim 22, and that claim 22 is directed to specific residues of SEQ ID NO: 2, not SEQ ID NO: 3. The specific residues of SEQ ID NO: 2 are disclosed in the Specification on page 2, lines 9-15. In regards to claims 28-32 and 34, these specific residues are disclosed in the Specification in three locations: 1) the residues 1-23 of SEQ ID NO: 3 are disclosed on page 2, lines 16- 20; 2) the residues 24-278 are also disclosed on page 2, lines 16-20; and 3) the isolated protein polypeptides that are substantially homologous to SEQ ID NO: 3 are disclosed on page 8, lines 18-20.

However, to expedite prosecution and allowance of present application, Applicants have cancelled claims 28-32 and 34. Applicants reserve the right to prosecute the subject matter of

claims 28-32 and 34 in a later application. Accordingly, in light of the above amendment, this rejection is now moot.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that the pending claims are in condition for allowance. If for any reason the Examiner feels that a telephone conference would expedite prosecution of the Application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

Dated: July 29, 2004

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Enclosures:

- Petition and Fee for Extension of Time (in duplicate)
- Amendment Fee Transmittal (in duplicate)
- 5 Cases Cited Herein
- Notice of Appeal
- Postcard

H:\Patents\Shelby\97-28\US\C1\Response to the January 29, 2004 Office Action.doc

*626 F.2d 853, *; 1980 CCPA LEXIS 212, **;*
206 U.S.P.Q. (BNA) 881

NORMAN A. NELSON, Appellant, v. BOWLER AND CROSSLEY, Appellees.

Appeal No. 79-630.

UNITED STATES COURT OF CUSTOMS AND PATENT APPEALS

626 F.2d 853; 1980 CCPA LEXIS 212; 206 U.S.P.Q. (BNA) 881

July 31, 1980, Decided; As Amended

PRIOR HISTORY: [1]**

Interference No. 98,926.

CASE SUMMARY

PROCEDURAL POSTURE: Appellant sought review of decision of the Board of Patent Interferences, awarding priority to appellee.

OVERVIEW: Appellant sought review of decision awarding priority to appellee. In determining utility, the court held it was unnecessary for appellant to establish a specific therapeutic use, but that evidence of any utility was sufficient. Adequate proof of any pharmacological activity constituted a showing of practical utility. The court held that tests conducted using 16-phenoxy-substituted prostaglandins manifested a practical utility. Tests demonstrated modulation of blood pressure and smooth muscle stimulation, similar to effect of natural prostaglandins, in laboratory test animals. The court also held that appellee failed to demonstrate, by clear and convincing evidence, that appellant committed fraud in his application. Speculative inaccuracies in appellant's alleged utilities amounted to, at most, simple negligence. Appellee failed to show clear intent by appellant to mislead patent examiner by false utility statements.

OUTCOME: The court reversed decision, as tests conducted using 16-phenoxy-substituted prostaglandins manifested a practical pharmacological utility, blood pressure modulation and smooth muscle stimulation, similar to that of natural prostaglandins. In determining utility, unnecessary for appellant to establish specific therapeutic use, but evidence of any pharmacological activity constituted showing of practical utility.

CORE TERMS: practical utility, compound, pharmacological, blood pressure, smooth muscle, correlation, stimulation, colon, rat, reduction, analog, pressor, gerbil, occurring, naturally, evidenced, biphasic, phenoxy, tested, pupil, assay, tetrabenazine, antagonism, recite, serial, anticholinergic, prostaglandins, modulation, depressor, dilation

LexisNexis(R) Headnotes ◆ Hide Headnotes

Patent Law > Utility Requirement > Proof of Utility

HN1 Evidence of any utility is sufficient when the counts do not recite any particular utility. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN2 Tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN3 Practical utility is a shorthand way of attributing real-world value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN4 Adequate proof of any pharmacological activity constitutes a showing of practical utility. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN5 A rigorous correlation is not necessary where the test for pharmacological activity is reasonably indicative of the desired response. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

Patent Law > Nonobviousness > Date of Invention

HN6 Whether a composition of matter must be tested in order to establish a reduction to practice, and if so, what tests are necessary, is a question which must be decided on the basis of the facts of the particular case involved. More Like This Headnote

Patent Law > Inequitable Conduct > Materiality, Scienter & Effect

Patent Law > Jurisdiction & Review > Standards of Review

HN7 Appellee must demonstrate that appellant committed fraud by clear and convincing evidence. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

Patent Law > U.S. Patent & Trademark Office Prosecution Procedures > Interferences

HN8 Every utility question arising in an interference must be decided on its own facts. Relevant evidence is judged as a whole for its persuasiveness in linking observed properties to suggested uses. Reasonable correlation between the two is sufficient for an actual reduction to practice. More Like This Headnote

COUNSEL: *Robert A. Armitage* and *Thomas J. Macpeak*, attorneys for appellant, *Peter D. Olexy* of counsel

Paul N. Kokulis attorney for appellee, *William T. Bullinger* and *J. D. Atkinson* of counsel

OPINIONBY: RICH

OPINION: [*854]

Before MARKEY, Chief Judge, RICH, BALDWIN, and MILLER, Associate Judges, and RE, Judge. *

* The Honorable Edward D. Re, Chief Judge, United States Customs Court, sitting by designation.

RICH, JUDGE.

This appeal is from the decision of the United States Patent and Trademark Office (PTO) Board of Patent Interferences (board) awarding priority on all four counts to Bowler et al. (Bowler), the senior party. We reverse.

This interference involves two applications, serial No. 252,030, filed by appellant Nelson May 10, 1972, for "Composition and Process" and serial No. 474,608, filed by Bowler May 30, 1974, as a

continuation of serial No. 248,717 filed April 28, 1972, for "Cyclopentane Derivatives." Appellee was accorded the benefit of an application filed in Great Britain on May 11, 1971, under 35 USC 119, and was designated senior party. Only Nelson took testimony.

The real parties in interest are Upjohn **[**2]** Company, assignee of Nelson, and Imperial Chemical Industries, Limited, assignee of Bowler.

The Subject Matter

Three counts remain in this appeal. n1/ Counts 2 and 4 describe 16-phenoxy-substituted prostaglandins (PG's) which are admitted to be structurally related to known, naturally-occurring prostaglandins commonly designated PGF2 alpha and PGE2.n2/ **[*855]** Count 1 is directed toward intermediates used to prepare the 16-phenoxy PG compounds of counts 2 and 4.

n1/ Count 3 employed compounds within count 2 in a method of inducing luteolysis (abortion caused by separation of the corpus luteum from the uterine wall). This count was expressly abandoned by Nelson at oral argument and in his brief.

n2/ "Natural prostaglandins" refers to PG's which have structures corresponding to those which occur in nature. While the art can synthesize natural PG's, the "natural" designation is retained to identify structure rather than origin.

Naturally occurring PG's allegedly had recognized value in pharmacology at the time the present invention was made. Both parties stated as much in their respective specifications. Effects such as smooth muscle stimulation and blood pressure **[**3]** modulation were said to be reflected in various commercial applications. For example, labor induction or abortion was attributed to uterine smooth muscle stimulation caused by administration of PG's. Modification of blood pressure, on the other hand, was purportedly useful in treating either shock or hypertension since natural PG's can either raise or lower blood pressure.

The Issue

The issue is whether Nelson has shown at least one utility for counts 1, 2, and 4 which sufficiently establishes an actual reduction to practice before the critical date of May 11, 1971. Specifically, is a practical utility manifested in testing 16-phenoxy PG's for their stimulation of smooth muscle tissue from gerbil colons and their modulation of blood pressure in rats?

The Evidence

Two tests conducted at Upjohn before the critical date are relied upon by appellant to prove practical utility. They are referred to as the rat blood pressure (BP) test and the gerbil colon smooth muscle stimulation (GC-SMS) test. The comparison standards for both were selected from naturally occurring PG's, i.e., PGF2 alpha and PGE1, having known blood pressure and smooth muscle stimulation responses.

In **[**4]** the BP test, the blood pressure of anesthetized rats recorded on a polygraph chart to determine whether an injected compound had any effect. Responses were categorized as either a depressor (lowering) effect or a pressor (elevating) effect. Calibration was supposedly achieved by comparing an unknown analog PG versus either a standard natural PG depressor, such as PGF1, or a standard natural PG pressor, such as PGE2. Each rat was given successive PG's to test. Allowance was made for the blood pressure to approach a normal level before administering another PG.

The tested compounds, labeled 38980 and 38669, were both reported to give an atypical or biphasic response. That is, both initially depressed the rat's blood pressure before raising it. The depressor effect was a temporary manifestation lasting several seconds. The subsequent

pressor effect, however, was a strong response lasting several hours. Nelson exhibits 27 and 28, the test results for the above-mentioned compounds, reflect an equivalent activity between the above analog compounds and the naturally occurring compounds.

During the testimony period of this interference, Dr. James Weeks, another Upjohn research **[**5]** scientist, was questioned about the reliability of the BP test. He answered that, as of April 1971, this test had been in use for between five and six years. In that period, he said it gave excellent results.

The GC-SMS test was in vitro as opposed to the in vivo BP test. Purportedly, Upjohn technicians excised a section of colon from a freshly-killed gerbil for suspension in a physiological solution. A lever arm was connected to the colon in such a way that any contraction was recorded as a polygraph trace. For comparison purposes, PGE, a known smooth muscle stimulant, was employed. Both of Nelson's tested analog compounds were said to closely approximate the response of the natural compounds.

Board Decision

Both conception and preparation by Nelson of compounds within the scope of counts 1, 2, and 4 were held to have occurred prior to the critical date. Since the counts did not recite any utility, the board declared that the 16-phenoxy PG's could have any practical utility, i.e., utility sufficient for an actual reduction to practice, citing Blicke v. Treves, 44 CCPA 753, 241 F.2d 718, 112 USPQ 472 (1957). But priority was not awarded to Nelson because his **[*856]** **[**6]** evidence was held not to show adequate proof of practical utility.

The tests used by Nelson were characterized as "rough screens, uncorrelated with actual utility." The board said neither the biphasic pressor effect in rats nor the stimulation of gerbil colon smooth muscle revealed a practical utility, citing Rey-Bellet v. Engelhardt, 493 F.2d 138, 181 USPQ 453 (CCPA 1974). The present situation was compared to that in Knapp v. Anderson, 477 F.2d 588, 177 USPQ 688 (CCPA 1973), where only a potential utility was established.

Finally, Nelson's conduct, as evidenced by statements in his application, was evaluated for inequitable conduct which might establish fraud. The clear and convincing proof necessary to establish fraud was held to be missing. The board stated that Bowler failed to show how Nelson had either misled the examiner or knowingly presented false information. Speculative statements of utility were found insufficient to establish inequitable conduct.

OPINION

Practical Utility

The board correctly stated that HN1 evidence of any utility is sufficient since the counts do not recite any particular utility. Blicke v. Treves, supra. However, we cannot agree with its conclusion **[**7]** that the pharmacological activity evidenced by the BP and the GC-SMS tests does not establish a practical utility. even though Nelson now admits that antifertility activity such as luteolysis is not proven by these tests, the board erred in not recognizing that HN2 tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use.

"Practical HN3 utility" is a shorthand way of attributing "real-world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.

Knowledge of the pharmacological activity of any compound is obviously beneficial to the public. It is inherenly faster and easier to combat illnesses and alleviate symptoms when the medical profession is armed with an arsenal of chemicals having known pharmacological activities. Since it is crucial to provide researchers with an incentive to disclose pharmacological activities in as many compounds as possible, we conclude that HN4 adequate proof of any such activity constitutes a showing of practical utility.

Bowler argues that the BP and GC-SMS tests **[**8]** are inconclusive showings of pharmacological activity since confirmation by statistically significant means, i.e., a 4-point assay, n4/ occurred after the critical date. But HN5 a rigorous correlation is not necessary where the test for pharmacological activity is reasonably indicative of the desired response. While Dr. Brown, an Upjohn PG researcher, testified that treatment of one muscle with various successive compounds, as done here, could involve a small residual carryover effect from one compound to another, he also indicated that the correlation between the "preliminary" test and 4-point assays was reasonably certain. In view of the above correlation, the 4-point assay, while preferable, was not the sole means for establishing practical utility.

n4/ A 4-point assay consists of testing one compound against one standard in either four rats or on four gerbil colons.

We also do not attach much significance to the atypical blood pressure response in the BP test. The record states that the biphasic nature was predominantly a sustained pressor effect, a known activity of certain natural PG's n5/ with established therapeutic uses. Nor are we concerned with the admitted variability **[**9]** of smooth muscle responses. Even with known PG's the response differs among smooth muscles. The controlling point is that these responses are evidence of pharmacological activity. As this court said in Blicke, supra,

n5/ In fact, Charles Lawson, an Upjohn research associate, stated that sometimes even PGF2 alpha manifested a biphasic effect. **[*857]**

* * * HN6 whether a composition of matter must be tested in order to establish a reduction to practice, and if so, what tests are necessary, is a question which must be decided on the basis of the facts of the particular case involved.

This appeal is not analogous, as the board suggests, to Rey-Bellet v. Engelhardt, supra, even though the issues are similar. There, a new drug, nortriptyline (NTL), and one of its known analogs, amitriptyline (N-methyl substituted NTL), were tested. The results were subsequently offered to prove practical utility for NTL. For example, the "General Mental Health Screening Test" was designed to check for "physical responses." The presence or absence of a response in a test animal after an injection could have indicated pharmacological activity.

The inherent lack of certainty in this test **[**10]** resulted in a failure to prove practical utility. while Engelhardt advocated that pupil dilation evidenced anticholinergic activity, n6/ this court did not find adequate correlation between them. The Mental Health test was found not to be specific for the claimed activity since drugs without that activity could have caused pupil dilation.

n6/ Anticholinergic action describes the blocking of neural impulses passing along the parasympathetic or autonomic nervous system which includes ocular nerves.

We specifically note that anticholinergic activity was the sole utility maintained by Engelhardt for the purposes of the Mental Health test. He did not argue that pupil dilation in itself was a useful pharmacological activity. Without such an argument, proof of pupil responses, alone, did not establish an actual reduction to practice.

Engelhardt also argued that since amitryptyline, a compound of proven utility, had a very close structural similarity to NTL and produced similar test results, the utility of NTL had been proved. However, the Mental Health test was found to be unsuitable for detecting any of the known useful pharmacological activities possessed by the analog. **[**11]** Thus Engelhardt's argument of utility based upon analog similarity was equally invalid because of inconclusive

proof.

Another test in Rey-Bellet, the "tetrabenazine antagonism" test, supposedly evidenced antidepressant activity. Mice tranquilized by tetrabenazine were said to simulate depressed humans and animals. Antagonizing or offsetting the transquilizer was interpreted as a sign of activity. n7/ This court concluded that insufficient experience with the test precluded a showing of "the necessary correlation between tetrabenazine antagonism in mice and antidepressant activity in man [or animals]." Rey-Bellet, 493 F.2d at 1384, 181 USPQ at 456.

n7/ Again, we note that tranquilizer antagonism alone was not argued to be a practical utility.

We find Rey-Bellet to be distinguishable on its facts. According to the present evidence, specific pharmacological activities, i.e., smooth muscle stimulation and blood pressure modulation, were recognized as practical utilities. These activities were directly measured by dispositive tests. In other words, one skilled in the art at the time the tests were performed would have been reasonably certain that 16-phenoxy PG's had **[**12]** practical utility.

Bowler urges that Knapp v. Anderson, supra, supports their contention that the instant tests were evidence only of potential utility. We disagree. The laboratory testing in Knapp was conducted outside the "intended functional setting" and was not related to pharmacological activity. A claimed amine was allegedly useful as an ashless dispersant in lubricants for internal combustion engines. This court found that one skilled in the art would not find a practical utility solely in the results of a benth test for sludge dispersancy. Nor could one reasonably predict a practical utility therefrom since the losing party failed to establish a correlation between performance in the bench test and that within an engine.

Here, however, a correlation between test results and pharmacological activities has **[*858]** been established. The BP test inherently was of such a nature since it is performed in vivo and directly evidences the claimed activity. While the GC-SMS test is in vitro, both parties admit that it adequately simulates in vivo colon smooth muscle stimulation.

Fraud

HN7 Bowler must demonstrate that Nelson committed fraud by clear and convincing evidence. **[**13]** Norton v. Curtiss, 57 CCPA 1384, 1408, 433 F.2d 779, 797, 167 USPQ 532, 546-47 (1970). We agree with the board that he has not carried this heavy burden.

While Bowler accurately states that an applicant must recite utility with as reasonable a certainty as possible, i.e., without total disregard of facts within his knowledge, the speculative inaccuracies in Nelson's alleged utilities amount at most to simple negligence. While we do not sanction the use of boilerplate utility disclosures without regard to known contrary facts, this alone is insufficient to support a charge of fraud. Nowhere does Bowler show a clear intent by Nelson to mislead the examiner by false utility statements.

Summary

In the final analysis, HN8 every utility question arising in an interference must be decided on its own facts. Relevant evidence is judged as a whole for its persuasiveness in linking observed properties to suggested uses. Reasonable correlation between the two is sufficient for an actual reduction to practice. For the above reasons, we hold that Nelson sustained his burden of proving a prior actual reduction to practice.

The decision of the board awarding priority on counts 1, 2, and **[**14]** 4 to Bowler is reversed.

REVERSED

*628 F.2d 1322, *; 1980 CCPA LEXIS 213, **;*
206 U.S.P.Q. (BNA) 885

IN RE GEORGES JOLLES

Appeal No. 80-510.

UNITED STATES COURT OF CUSTOMS AND PATENT APPEALS

628 F.2d 1322; 1980 CCPA LEXIS 213; 206 U.S.P.Q. (BNA) 885

July 31, 1980, Decided

PRIOR HISTORY: [1]**

Serial No. 652,848.

CASE SUMMARY

PROCEDURAL POSTURE: Appellant sought review of the decision of the Patent and Trademark Office Board of Appeals affirming the examiner's rejection of appellant's patent claims under 35 U.S.C.S. § 101 and 35 U.S.C.S. § 112.

OVERVIEW: Appellant's patent claims encompassed drugs and methods useful for the treatment of acute myeloblastic leukemia in humans. Declarations in the claims reported that the drugs and methods resulted in 53 of 100 patients achieving complete remission and success in experimental testing with mice. The patent examiner rejected the claims under 35 U.S.C.S. § 101 and 35 U.S.C.S. § 112 for lack of utility and failure to show safety and effectiveness. The board held the experimental testing was not relevant to human utility. On appeal to the court, the dispositive issue was whether appellant had submitted sufficient evidence of the compositions and methods of the rejected claims for the treatment in human patients. The court held appellant's compounds had a close relationship to known drugs effective in cancer chemotherapy and that one of ordinary skill in the art would accept appellant's claimed utility in humans as valid and correct.

OUTCOME: The court reversed, holding that appellant had submitted sufficient evidence to establish the utility of the compositions and methods for the treatment of acute myeloblastic leukemia in humans.

CORE TERMS: composition, compound, declaration, examiner, myeloblastic, acute, patient, derivative, leukemia, naphthacene, experimental, patent, tested, dosage, mice, pharmaceutical, incredible, leukaemia, invention, alkanoyl, operativeness, animal, daunorubicin, doxorubicin, ingredient, clinical, carbon, atoms, effective, safe

LexisNexis(R) Headnotes ◆ Hide Headnotes

Patent Law > Patentable Subject Matter > Processes
HN1 See 35 U.S.C.S. § 101.

Patent Law > Specification & Claims > Definiteness
HN2 See 35 U.S.C.S. § 112.

Patent Law > Utility Requirement > Proof of Utility
HN3 Absence of asserted utility may lead to a rejection under either 35 U.S.C.S. § 101 or 35 U.S.C.S. § 112. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN4 Proof of utility is sufficient if it is convincing to one of ordinary skill in the art. The amount of evidence required depends on the facts of each individual case. The character and amount of evidence needed may vary, depending on whether the alleged utility appears to accord with or to contravene established scientific principles and beliefs. More Like This Headnote

COUNSEL: *Ellsworth H. Mosher*, attorney of record for appellant, *Charles A. Wendel Harold C. Wegner* of counsel.

Joseph F. Nakamura, for the Commissioner of Patents and Trademarks *Gerald H. Bjorge* of counsel.

OPINIONBY: BALDWIN

OPINION: [*1322]

Before MARKEY, Chief Judge, RICH, BALDWIN and MILLER, Associate Judges, and FORD, Judge. *

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* The Honorable Morgan Ford, United States Customs Court, sitting by designation.

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BALDWIN, Judge.

This appeal is from the decision of the Patent and Trademark Office Board of Appeals (board) affirming the examiner's rejection of claims 7-14, 16, 27-34 and 36 n1/ under 35 USC 101 n2/ and 35 USC 112, first paragraph, n3/ for lack of proof of utility. We reverse.

- - - - - - - - - - - - - - - Footnotes - - - - - - - - - - - - - - -

n1/ The claims appear in application Serial No. 652,848 (subject application), filed January 27, 1976, and entitled "Naphthacene Derivatives." The application is a division of Serial No. 307,955, filed November 20, 1972, now Patent No. 3,965,088, which in turn is a continuation-in-part of Serial No. 187,559, filed October 7, 1971, now Patent No. 3,957,755, which in turn is a continuation-in-part of Serial No. 768,532, filed October 17, 1968, now abandoned. **[**2]**

n2/ HN1☐ 35 USC 101 provides:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

n3/ HN2☐ 35 USC 112, first paragraph, provides:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any

person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

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Background

Composition claims 7-14 and 16 encompass certain pharmaceutical compositions **[*1323]** useful for the treatment of acute myeloblastic leukemia which comprise certain naphthacene derivatives. Method claims 27-34 and 36 encompass methods for the treatment of acute myeloblastic leukemia in a human patient by administering the subject naphthacene derivatives. Claims to the derivatives **[**3]** per se have been allowed in Patents No. 3,965,088 and 3,957,755.n4/

- - - - - - - - - - - - - - - Footnotes - - - - - - - - - - - - - - -

n4/ Seen.1 supra.

- - - - - - - - - - - - End Footnotes- - - - - - - - - - - - - -

The invention is represented by generic claims 7 and 28, reproduced below. As stated explicitly in the method claims, and as recognized by appellant in his brief, the compositions are intended for use in the treatment of acute myeloblastic leukemia in human patients.

7. A pharmaceutical composition for parenteral administration and useful for the treatment of acute myeloblastic leukaemia which comprises, as active ingredient, a naphthacene of the formula:

[See Illustration in Original]
wherein one of R1 and R2is oxygen and the other is oxygen or = N - NHR3, and R3 is alkanoyl of up to 4 carbon atoms, alkanoyl of up to 4 carbonatoms substituted by a sulphonic acid group, alkanoyl of up to 4 carbon atoms substituted by a quaternary ammonium group, thiocarbamoyl, methylthio-carbamoyl, amidino, or benzoyl,or a non-toxic salt thereof, in association with a significant amount of a sterile injectable pharmaceutically-acceptable **[**4]** carrier.

28. Method for the treatment of acute myeloblastic leukaemia in a human patient which comprises administering parenterally to the patient a quantity of from 2 to 10mg/kg per day of a naphthacene of the formula:

[See Illustration in Original]
wherein one of R1 and R2 is oxygen and the other is oxygen or = N - NHR3, and R3 is alkanoyl of up to 4 carbon atoms, alkanoyl of up to 4 carbon atoms substituted by a sulphonic acid group, alkanoyl of up to 4 carbon atoms substituted by a quarternary ammonium group, thiocarbamoyl, amidino, or benzoyl, or a non-toxic salt thereof.

The derivatives bear a close structural relationship to daunorubicin n5/ and doxorubicin, n6/ both of which are well recognized in the art as valuable for use in cancer chemotherapy. n7/

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n5/ Daunorubicin:

[See Illustration in Original]

n6/ Doxorubicin, also referred to asadriamycin, U.S. Patent

[See Illustration in Original]

n7/ The Merck index refers to each of these as "antineoplastic," i.e., antagonistic with respect to the formation of new growths.

- - - - - - - - - - - - End Footnotes- - - - - - - - - - - - - - **[**5]**

Affidavit Evidence
Jacquillat Declarations

Two declarations by Dr. Claude Jacquillat were submitted in application Serial No. **[*1324]** 187,559, and were before the examiner and the board in the prosecution of the subject application. Both declarations report results of clinical treatment of human patients suffering from acute myeloblastic leukemia with one of the claimed compositions. n8/ The second declaration dated January 3, 1974, reports results of treatment of 100 patients under the personal supervision of Dr. Jacquillat and the method of diagnosis of acute myeloblastic leukemia, and includes the results of the treatment of 33 patients reported in the first declaration dated August 28, 1972. Dr. Jacquillat outlined the dosage rate, the length of dosage, and methods of evaluating its effect through daily blood counts and periodic bone marrow examination. Among the results reported, complete remission of the disease was achieved in 53 of the patients treated. Dr. Jacquillat concluded that the specific composition used is an active drug in the treatment of acute myeloblastic leukemia and is a valuable addition to the series of drugs available for such treatment. **[**6]**

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n8/ Claims 15 and 35, which stand allowed, are directed to the specific pharmaceutical composition and corresponding method for treatment reported by Dr. Jacquillat in his declarations. Claim 15 reads:

15. A composition according to Claim 7 in which active ingredient is 4-methoxy-5, 12-dioxo-6, 9, 11-trihydroxy-7-(2, 3, 3-0-tridesoxy-3-amino-1-L-lyxohexosyl)-9-[1-(benzoylhydrazono) ethyl]-5,7, 8, 9, 10, 12-hexahydronaphthacene, or a non-toxic acid addition salt thereof.

- - - - - - - - - - - - End Footnotes- - - - - - - - - - - - - -Maral Declarations

Two declarations by Dr. Rene Maral were before the examiner and the board in the prosecution of the subject application. The first declaration, dated January 22, 1971, in application Serial No. 768,532, disclosed results of experimental tests with laboratory mice wherein tests for sub-acute toxicity, activity against sarcoma 180 tumors, and activity against leukemiaL 1210 of seven specific compositions were reported. The compositions tested were those described in examples 1-7 of the subject application. The seventh **[**7]** composition was the same composition utilized in the Jacquillat clinical tests. See n.8 supra. On the basis of reported results, Dr. Maral concluded that "the compounds of * * * Application Serial No. 768,532 have substantial activity against experimental tumours in mice in tests customarily used for the screening of anti-cancer agents of potential utility in the treatment of humans."

The second declaration, dated January 31, 1975, in application Serial No. 307,955, disclosed similar results from the same tests for sub-acute toxicity and anti-tumor activity for an additional composition corresponding to that described in example 8 of the subject application. On the basis of reported results, Dr. Maral concluded that the specific composition tested "has a

substantial activity against experimental tumours in mice in tests customarily used for the screening of anti-cancer agents of potential utility in the treatment of humans."

The eight compounds tested by Dr. Maral are structurally related, the differences residing in the second C9 substituent, being other than a hydroxy group. See claims 7 and 28 supra. Appellant provided the following tabulation of differences for the eight **[**8]** compounds tested.

Species Composition Claim	Species Method Claim	The Second C, Substituent
9	29	1-(3-sulphopropionyl-hydrazono) ethyl
10	30	1-(trimethyl-ammonio-acetylhydrazono) ethyl
11 *	31 *	1-(thiosemicarbazono) ethyl
12	32	1-(amidino-hydrazono) ethyl
13 *	33 *	1-(thiosemicarbazono) ethyl
14	34	1-(4-methylthiosemicarbazono) ethyl
15	35	1-(benzoylhydrazono)-ethyl
16	36	1-(formylhydrazono) ethyl

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* Here the second C9 substituent is the same, but the claims differ slightly in the naphthacene nucleus in that in the active ingredient recited in the latter pair of claims only one oxo (O) need be present at the C5 and C12 positions.

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The Rejection

The examiner, relying on no prior art, rejected claims 7-16 and 27-36under 35 USC 101 and 35 USC 112, first paragraph, "for lack of proof of utility." **[*1325]** The examiner, in her answer, found there was "insufficient evidence of operativeness in the record that the various compositions are safe **[**9]** and effective to treat acute myeloblastic leukaemia in human patients," citing In re Citron, 51 CCPA 852, 325 F.2d 248, 139 USPQ 516 (1963), for support. The examiner further asserted:

The instant claims are directed to an incredible utility. The method of treating a human leukaemia and a pharmaceutical composition for this use employing appellant's naphthacene compounds have not been set forth in the specification as required by the statute. There are no specific examples or test data showing the effectiveness of the claimed pharmaceutical compositions for the alleged use which would include a specific dosage for a specific patient and duration of treatment. The dosage range given for the active ingredient, i.e. the naphthacene compound in the composition is 2-10 mg./kg. per day. It is not stated in the specification, however, whether the dosage should be given periodically or in a single does, nor what a total dosage should be. Accordingly, appellant has not made known exactly how his invention is to be used, but rather, has left the matter of how to use to speculation. * * *

The Declaration of Dr. Jacquillat * * * has again been carefully considered, but is not convincing. **[**10]** The Declaration shows the use of only one of the compounds used in appellant's invention, which is the pharmaceutical composition of claim 15 and the method of claim 35. This compound is referred to as product "g" in the Declaration which shows that out of 100 patients treated with product "g", only 53 (53%) had complete remission after 30 to 40 days of treatment ** *. The remission was not of long duration as shown in Table II of the Declaration. Table I of the Declaration shows that death occurred in thirteen adults during induction of the treatment. Therefore, this data is not deemed persuasive that product "g", the compound used in claims 15 and 35, is safe and effective for treating acute myeloblastic leukaemia in humans.

With regard to the various other naphthacene compounds employed in appellant's methods and compositions of claims 7-14, 16-34 and 36, due to the unpredictability of chemical compounds and side reactions, and therapeutic conditions such as leukaemia, it would not be reasonable for a person of ordinary skill in the art to presume that these novel compounds would be safe and effective for the incredibleutility alleged in the absence of verified data substantiating **[**11]** the said allegations of use.

The Board

The board sustained the rejection of claims 7-14, 16, 27-34 and 36 but not the rejection of claims 15 and 35. The board reasoned as follows:

We have carefully considered all of the arguments and evidence and conclude that the results set forth in the Maral declaration exhibit effectiveness for each of the claimed compositions with respect to the treatment of experimental tumors, i.e., sarcoma 180 and leukemia L1210 in mice and hence establish the utility of the compositions in mice. * * * We think it is clear from appellant's remarks that the present claims on appeal contemplate only human utility. In that regard, the Maral evidence is not relevant.

With respect to the additional evidence set forth in the declarations of Professor Jacquillat regarding the treatment of humans afflicted with acute myeloblastic leukemia, we find that only one compound was tested relating to the operativeness of the claimed subject matter. In carefully evaluating the Jacquillat evidence, we observe that the active ingredient of claims 15 and 35 administered in the manner taught in the specification is useful to some degree inasmuch as remissions in 53% **[**12]** of the patients were achieved and we therefore conclude that the operativeness of said compound is sufficiently established to satisfy the requirements of 35 USC 101 and the first paragraph of **[*1326]** 35 USC 112. With respect to the Examiner's contention that it has not been demonstrated that the claimed invention is safe, we refer to In re Anthony, 56 CCPA 1443, 414 F.2d 1383, 162 USPQ 594 (1969) and In re Watson, 517 F.2d 465, 186 USPQ 11 (CCPA 1975) which hold that claims may satisfy the requirements of 35 USC 101 for utility despite the lack of safety. * * *

The Jacquillat evidence, however, which is limited to one compound is insufficient to satisfy the requirements of 35 USC 101 with respect to the remaining claims in view of the nature of the utility and the scope of the claims. There is no indication that the compounds of claims 7 to 14, 16, 27 to 34 and 36 which differ in structure from the benzoyl-hydrazono compound of claims 15 and 35 are effective in the treatment of acute myeloblastic leukemia.

Appellant appears to rely upon the analogy with the known compounds "daunorubicin and doxorubicin"to provide the utility requirements for all of the compositions. The **[**13]** claimed products differ from the aforesaid prior art compounds in the replacement of keto groups at C-9 and/or at one of C-5 and C-12 positions with an =N-NH-R3 grouping, wherein R3 is set forth as a variety of substituents. We note that the Examiner has reviewed the prior art as represented by the Arcamone et al. patents [n10/] and determined that the claimed compositions were not prima facie obvious therefrom. We cannot conclude that the claimed compositions are so similar to those of the prior art as to expectedly have the same specific utility of treating acute myeloblastic leukemia in humans. On the record before us, considering the nature of the stated

utility, we cannot conclude that appellant has submitted sufficient evidence of demonstrated utility commensurate with the scope of the claims. We find the quantum of evidence represented by a single compound falls far short in proving the asserted utility.

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n10/ The Arcamone et al. patents, U.S. Patents No. 3,590,028 and 3,686,163, were cited as prior art references in the prosecution of U.S. Patents No. 3,957,755 and 3,965,088, wherein claims for the naphthacene derivative compositions per se were allowed. See n.1 supra.

- - - - - - - - - - - - - End Footnotes- - - - - - - - - - - - - - **[**14]**

OPINION

While the rejection below was under both 35 USC 101 and 35 USC 112, first paragraph, the dispositive issue is whether appellant has submitted sufficient evidence to establish his asserted utility of the compositions and methods of the rejected claims for the treatment of acute myeloblastic leukemia in human patients. n11/ The examiner in her rejection raised questions on the legal adequacy of appellant's disclosure of how to use the claimed compounds under 35 USC 112, first paragraph, viz., the specific dosage and duration of treatment, but the board has specifically rejected this argument with regard to claims 15 and 35, and the solicitor does not argue this further in his brief. Accordingly, we consider the rejection under both provisions to turn on the proof of utility issue.

- - - - - - - - - - - - - - Footnotes - - - - - - - - - - - - - -

n11/ HN3 Absence of asserted utility may lead to a rejection under either 35 USC 101 or 35 USC 112. In re Gardner, 475 F.2d 1389, 1392, 177 USPQ 396, 398 (CCPA 1973).

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The contents of the declarations in the record and the **[**15]** qualifications of the declarants have not been challenged, so we accept their contents and conclusions at face value.HN4

Proofof utility is sufficient if it is convincing to one of ordinary skill in the art. In re Irons, 52 CCPA 938, 340 F.2d 974, 144 USPQ 351 (1965). The amount of evidence required depends on the facts of each individual case. In re Gazave, 54 CCPA 1524, 379 F.2d 973, 154 USPQ 92 (1967). The character and amount of evidence needed may vary, depending on whether the alleged utility appears to accord with or to contravene established scientific principles and beliefs. In re Chilowsky, 43 CCPA 775, 229 F.2d 457, 108 USPQ 321 (1956). **[*1327]**

The examiner in her rejection referred to the "incredible utility" of the subject claims. The solicitor in his brief further argues that "[at] best the asserted usefulness here is highly speculative and against the grain of human experience. At worst it is incredible." Neither the solicitor nor the examiner provides support for the assertion regarding "incredible utility." Such assertions have been readily rebutted by the Jacquillat evidence together with the known utility of daunorubicin and doxorubicin, which clearly **[**16]** establish that the medical treatment of a specific cancer is not such an inherently undelievable undertaking or involves such implausible scientific principles as to be considered incredible.

The board avoided the examiner's assertion of incredible utility, but did question the operativeness of the claimed subject matter. When utility as a drug, medicant, and the like in human therapy is alleged, it is proper for the examiner to ask for substantiating evidence unless one with ordinary skill in the art would accept the allegations as obviously correct. In re Novak, 49 CCPA 1283, 306 F.2d924, 134 USPQ 335 (1962).

However, in considering the evidence proffered by appellant, the board dismissed the Maraldeclarations as not relevant to establish the claimed human utility. The Jacquillat clinical tests were accepted by the board solely for the establishment of utility for the specific composition tested.

We believe the board erred in dismissing the Maral evidence as not relevant to human utility. This court recognizes "that a demonstration that a compound has desirable or beneficial properties in the prevention, alleviation, or cure of some disease or manifestation of a disease **[**17]** in experimental animals does not necessarily mean that the compound will have the same properties when used with humans." In re Krimmel, 48 CCPA 1116, 1123, 292 F.2d 948, 953, 130 USPQ 215, 219 (1961). However, this is by no means support for the board's position that such evidence is not relevant to human utility.

To the contrary, this court has accepted tests on experimental animals as sufficient to establish utility in In re Bergel, 48 CCPA 1102, 292 F.2d 955, 130 USPQ 206 (1961). Utility was recognized by this court in Bergel not because of any concern with the health or existence of the experimental animals, but rather because of the widespread pharmacological work in animals recognized as a screening procedure for testing new drugs. It is clear that such testing is relevant to utility in humans. Evidence showing substantial activity against experimental tumors in mice in tests customarily used for the screening of anti-cancer agents of potential utility in the treatment of humans is relevant to utility in humans and is not to be disregarded. In re Buting, 57 CCPA 777, 418 F.2d 540, 163USPQ 689 (1969).

The board, after evaluating the Jacquillat evidence, concluded that **[**18]** the operativeness of the specific derivative utilized in the Jacquillat clinical tests was sufficiently established to satisfy the utility requirements of sections 101 and 112, first paragraph, and accordingly did not sustain the examiner's rejection of claims 15 and 35. However, the board found the quantum of evidence represented by the single derivative to fall far short in proving the asserted utility for the remaining claimed derivatives. The board erred in this finding by failing to give sufficient weight to the similarity of the remaining claimed derivatives to the derivative in allowed claims 15 and 35 when considered with the Maral animal tests.

The similarities of the claimed derivatives to each other are represented in the tabulation of differences provided supra for the eight compounds tested by Dr. Maral. The Maral declarations establish that the eight compounds have substantial activity against experimental tumors in mice. The board found that the successful clinical tests in humans of the one derivative shown in the Jacquillat declarations sufficiently established utility for claims 15 and 35. The claimed compounds have a close structural relationship to daunorubicin **[**19]** and doxorubicin, both known to be useful in cancer chemotherapy. Considering these facts in the record before us, we conclude that one **[*1328]** of ordinary skill in the art would accept appellant's claimed utility in humans as valid and correct.

The decision of the board is reversed.

REVERSED

*383 U.S. 519, *; 86 S. Ct. 1033, **;*
*16 L. Ed. 2d 69, ***; 1966 U.S. LEXIS 2907*

BRENNER, COMMISSIONER OF PATENTS v. MANSON

No. 58

SUPREME COURT OF THE UNITED STATES

383 U.S. 519; 86 S. Ct. 1033; 16 L. Ed. 2d 69; 1966 U.S. LEXIS 2907; 148 U.S.P.Q. (BNA) 689

November 17, 1965, Argued
March 21, 1966, Decided

PRIOR HISTORY:

CERTIORARI TO THE UNITED STATES COURT OF CUSTOMS AND PATENT APPEALS.

DISPOSITION: 52 C. C. P. A. (Pat.) 739, 333 F.2d 234, reversed.

CASE SUMMARY

PROCEDURAL POSTURE: Petitioner Commissioner of Patents sought certiorari review of a judgment from the United States Court of Customs and Patent Appeals, which granted respondent a declaration of interference premised on a holding that, in the chemical patent field, where a claimed process produced a known product, it was not necessary to show utility of the product so long as the product was not alleged to be detrimental to the public interest.

OVERVIEW: Petitioner Commissioner of Patents sought review of a judgment that respondent was entitled a declaration of interference, premised on a holding that, in the chemical field, where a claimed process produced a known product it was not necessary to show utility of the product so long as the product was not alleged to be detrimental to the public interest. Because the Court of Customs and Patent Appeals (CCPA) was a court established under U.S. Const. art. III, the United States Supreme Court held the CCPA exercised judicial, not administrative power, and the Court had jurisdiction, under 28 U.S.C.S. § 1256, to review decisions of the CCPA. The Court held the issue of patentability had to be settled before an interference was declared, and under 35 U.S.C.S. § 101, respondent was entitled to patent only that which was useful. The Court further held that because no patent could be granted on a chemical compound whose sole utility was its potential role as an object of use-testing, no patent could be granted on the process that yielded the unpatentable product. Accordingly, the judgment granting respondent a declaration of interference was reversed.

OUTCOME: The Court reversed the judgment granting respondent a declaration of interference because the issue of patentability of respondent's claimed process had to be resolved before an interference was declared, and respondent's claimed process was not patentable where it yielded a chemical compound whose sole utility was its potential role as an object of use-testing.

CORE TERMS: patent, chemical, compound, patentability, invention, steroid, disclosure, yielded, inventor, homologue, adjacent, disclose, filing date, scientific, monopoly, patentee, discovery, statutory scheme, patentable, public interest, tumor-inhibiting, detrimental, usefulness, secrecy, chemist, unpatentable, infringement, unqualified, declaration, trademark

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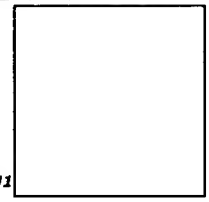
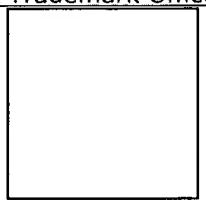
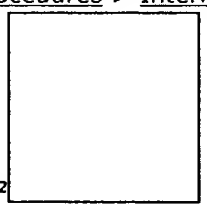
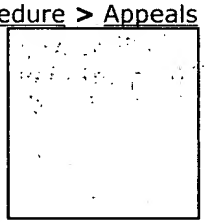
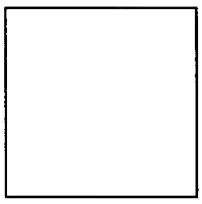
Patent Law > U.S. Patent & Trademark Office Prosecution Procedures > Interferences 

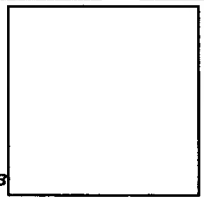
HN1 See 35 U.S.C. § 135.

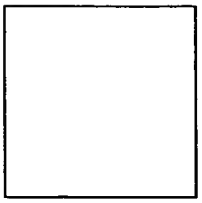
Patent Law > U.S. Patent & Trademark Office Prosecution Procedures > Interferences 

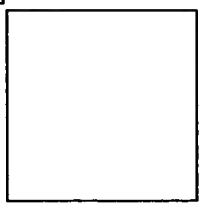
HN2  See 37 C.F.R. § 1.204(b).

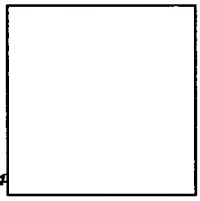
Civil Procedure > Appeals > U.S. Supreme Court Review > Federal Court Decisions 

Patent Law > Jurisdiction & Review > Subject Matter Jurisdiction 

HN3  28 U.S.C.S. § 1256 provides that cases in the Court of Customs and Patent Appeals may be reviewed by the United States Supreme Court by writ of certiorari. More Like This Headnote

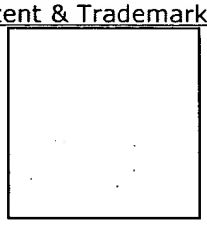
Constitutional Law > The Judiciary > Jurisdiction 

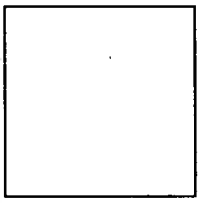
Patent Law > Jurisdiction & Review > Subject Matter Jurisdiction 

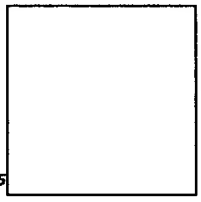


HN4 The Court of Customs and Patent Appeals is a court established under U.S. Const. art. III, that is, a constitutional court exercising judicial rather than administrative power. 28 U.S.C.S. § 211. More Like This Headnote

Patent Law > U.S. Patent & Trademark Office Prosecution

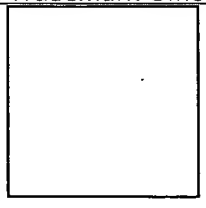
Procedures > Appeals 

Patent Law > Jurisdiction & Review > Subject Matter Jurisdiction 



HN5 Determinations of the United States Patent and Trademark Office may be challenged either by appeal to the Court of Customs and Patent Appeals or by suit instituted in the United States District Court for the District of Columbia. 35 U.S.C.S. § 145, 28 U.S.C.S. § 1542. Where the latter route is elected, the decision obtained may be reviewed in the Court of Appeals for the District of Columbia Circuit, and ultimately in the United States Supreme Court upon writ of certiorari. More Like This Headnote

Patent Law > U.S. Patent & Trademark Office Prosecution

Procedures > Interferences 

HN6 37 C.F.R. § 1.201(a) defines an interference proceeding as one involving two or more parties claiming substantially the same patentable invention and may be instituted as soon as it is determined that common patentable subject matter is claimed. The question as to patentability of claims to an applicant must be determined before any question of interference arises and claims otherwise unpatentable to an applicant cannot be allowed merely in order to set up an interference. More Like This Headnote

Patent Law > U.S. Patent & Trademark Office Prosecution

Procedures > Interferences

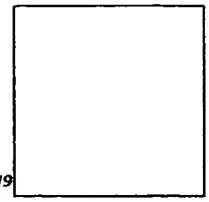
HN7 37 C.F.R. § 1.203(a) makes it explicit that an examiner, before a declaration of interference, must determine the patentability of a claim as to each party. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

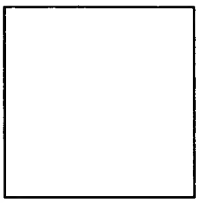
HN8 One may patent only that which is "useful." More Like This Headnote

Patent Law > Patentable Subject Matter > Processes

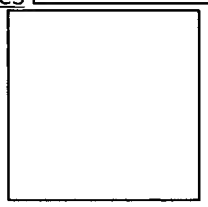
Patent Law > Utility Requirement > Proof of Utility



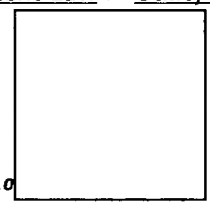
HN9 See 35 U.S.C.S. § 101.



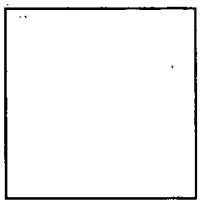
Patent Law > Patentable Subject Matter > Processes



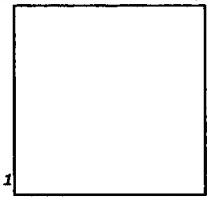
Patent Law > Utility Requirement > Proof of Utility



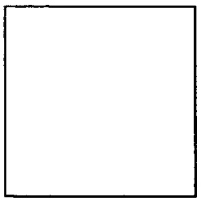
HN10 Unless and until a process is refined and developed to a point where specific benefit exists in a currently available form there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. More Like This Headnote



Patent Law > Utility Requirement > Chemical Compounds



HN11 A patent system must be related to the world of commerce rather than to the realm of philosophy. More Like This Headnote



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SYLLABUS: In December 1957 Ringold and Rosenkranz applied for a patent on an allegedly novel process for making certain steroids, claiming priority as of December 1956. A patent issued thereon in 1959. In January 1960 respondent filed an application to patent the same process, asserting that he had discovered it prior to December 1956, and requesting that an "interference" be declared to test the issue of priority. Respondent's application was denied by a Patent Office examiner, the Board of Appeals affirming, for failure "to disclose any utility for"

the compound produced by the process. The Court of Customs and Patent Appeals (CCPA) reversed, holding that "where a claimed process produces a known product it is not necessary to show utility for the product" as long as it is not detrimental to the public interest. *Held*:

1. This Court has jurisdiction under 28 U. S. C. § 1256 to review upon petition of the Commissioner of Patents patent decisions of the CCPA. Pp. 523-528.

2. The Patent Office properly may refuse to declare an "interference" on the ground that the application therefor fails to disclose a prima facie case of patentability. P. 528, n. 12.

3. The practical utility of the compound produced by a chemical process is an essential element in establishing a prima facie case for the patentability of the process. Pp. 528-536.

(a) One may patent only that which is useful. Pp. 528-529, 535.

(b) Respondent has not provided any basis for overturning the determination of the Patent Office that the utility requirement was not satisfied in this case by reference to the alleged utility of an adjacent homologue. Pp. 531-532.

(c) The requirement that a chemical process be useful is not satisfied by a showing that the compound yielded belongs to a class of compounds which scientists are screening for possible uses. Pp. 532-536.

(d) Nor is the utility requirement for chemical processes satisfied by a showing that the process works, *i. e.*, yields the intended product. Pp. 532-536.

COUNSEL: Paul Bender argued the cause for petitioner, pro hac vice, by special leave of Court. With him on the brief were Solicitor General Marshall, Assistant Attorney General Douglas, Sherman L. Cohn and Edward Berlin.

Dean Laurence argued the cause for respondent. With him on the brief were Herbert I. Sherman and John L. White.

W. Brown Morton, Jr., and Ellsworth H. Mosher filed a brief for the American Patent Law Association, as amicus curiae, urging affirmance.

JUDGES: Warren, Fortas, Harlan, Brennan, Black, Stewart, Clark, White, Douglas

OPINIONBY: FORTAS

OPINION: [*520] [*72] [**1034]** MR. JUSTICE FORTAS delivered the opinion of the Court.

This case presents two questions of importance to the administration of the patent laws: First, whether this Court has certiorari jurisdiction, upon petition of the Commissioner of Patents, to review decisions of the Court of Customs and Patent Appeals; and second, whether the practical utility of the compound produced by a chemical process is an essential element in establishing a prima facie case for the patentability of the process. The facts are as follows:

In December 1957, Howard Ringold and George Rosenkranz applied for a patent on an allegedly novel process for making certain known steroids. n1 They claimed **[*521]** priority as of December 17, 1956, the date on which they had filed for a Mexican patent. United States Patent No. 2,908,693 issued late in 1959.

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n1 The applicants described the products of their process as "2-methyl dihydrotestosterone derivatives and esters thereof as well as 2-methyl dihydrotestosterone derivatives having a C-

17 lower alkyl group. The products of the process of the present invention have a useful high anabolic-androgenic ratio and are especially valuable for treatment of those ailments where anabolic or antiestrogenic effect together with a lesser androgenic effect is desired."

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In January 1960, respondent Manson, a chemist engaged in steroid research, filed an application to patent precisely the same process described by Ringold and Rosenkranz. He asserted that it was he who had discovered the process, **[**1035]** and that he had done so before December 17, 1956. Accordingly, he requested that an "interference" be declared in order to try out the issue of priority between his claim and that of Ringold and Rosenkranz. n2

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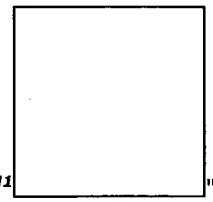

n2 35 U. S. C. § 135 (1964 ed.) provides: HN1 "Whenever an application is made for a patent which, in the opinion of the Commissioner, would interfere with any pending application, or with any unexpired patent, he shall give notice thereof . . . . The question of priority of invention shall be determined by a board of patent interferences . . . whose decision, if adverse to the claim of an applicant, shall constitute the final refusal by the Patent Office of the claims involved, and the Commissioner may issue a patent to the applicant who is adjudged the prior inventor. . . ."
title." n14
"https://www.lexis.com/research/" \l "clscc2" \t "_self" HN2 Patent Office Rule 204 (b), 37 CFR § 1.204 (b), provides: "When the filing date or effective filing date of an applicant is subsequent to the filing date of a patentee, the applicant, before an interference will be declared, shall file an affidavit that he made the invention in controversy in this country, before the filing date of the patentee . . . and, when required, the applicant shall file an affidavit . . . setting forth facts which would prima facie entitle him to an award of priority relative to the filing date of the patentee."

Judge Thurman Arnold has provided an irreverent description of the way patent claims, including "interferences," are presented to the Patent Office. See *Monsanto Chemical Co.* v. *Coe*, 79 U. S. App. D. C. 155, 145 F.2d 18.

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A Patent Office examiner denied Manson's application, and the denial was affirmed by the Board of Appeals within the Patent Office. The ground for rejection was the failure "to disclose any utility for" the chemical compound produced by the process. Letter of Examiner, dated May 24, 1960. This omission was not **[*522]** cured, in the opinion of the Patent Office, by Manson's reference to an article in the November 1956 issue of the Journal of Organic Chemistry, 21 J. Org. Chem. 1333-1335, which revealed that steroids of a class which included the compound **[***73]** in question were undergoing screening for possible tumor-inhibiting effects in mice, and that a homologue n3 adjacent to Manson's steroid had proven effective in that role. Said the Board of Appeals, "It is our view that the statutory requirement of usefulness of a product cannot be presumed merely because it happens to be closely related to another compound which is known to be useful."

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n3 "A homologous series is a family of chemically related compounds, the composition of which varies from member to member by CH[2] (one atom of carbon and two atoms of hydrogen). . . . Chemists knowing the properties of one member of a series would in general know what to expect in adjacent members." *Application of Henze*, 37 C. C. P. A. (Pat.) 1009, 1014, 181 F.2d 196, 200-201. See also *In re Hass*, 31 C. C. P. A. (Pat.) 895, 901, 141 F.2d 122, 125; *Application of Norris*, 37 C. C. P. A. (Pat.) 876, 179 F.2d 970; *Application of Jones*, 32 C. C. P. A. (Pat.) 1020, 149 F.2d 501. With respect to the inferior predictability of steroid homologues, see, *infra*, p. 532.

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The Court of Customs and Patent Appeals (hereinafter CCPA) reversed, Chief Judge Worley dissenting. 52 C. C. P. A. (Pat.) 739, 745, 333 F.2d 234, 237-238. The court held that Manson was entitled to a declaration of interference since "where a claimed process produces a known product it is not necessary to show utility for the product," so long as the product "is not alleged to be detrimental to the public interest." Certiorari was granted, 380 U.S. 971, to resolve this running dispute over what constitutes "utility" in chemical process claims, n4 as well as to answer the question concerning our certiorari jurisdiction.

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n4 In addition to the clear conflict between the Patent Office and the CCPA, there arguably exists one between the CCPA and the Court of Appeals for the District of Columbia. See *Petrocarbon Limited* v. *Watson*, 101 U. S. App. D. C. 214, 247 F.2d 800, cert. denied, 355 U.S. 955. But see *Application of Szwarc*, 50 C. C. P. A. (Pat.) 1571, 1576-1583, 319 F.2d 277, 281-286.

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[*523] I.

[1036]**

[*HR1]** [1]
Section 1256 of Title 28 U. S. C. (1964 ed.), enacted in 1948, ***HN3***provides that "Cases in the Court of Customs and Patent Appeals may be reviewed by the Supreme Court by writ of certiorari." This unqualified language would seem to foreclose any challenge to our jurisdiction in the present case. Both the Government n5 and the respondent urge that we have certiorari jurisdiction over patent decisions of the CCPA, although the latter would confine our jurisdiction to those petitions filed by dissatisfied applicants and would deny the Commissioner of Patents the right to seek certiorari. n6 This concert of opinion does not settle the basic question because jurisdiction **[***74]** cannot be conferred by consent of the parties. The doubt that does exist stems from a decision of this **[*524]** Court, rendered in January 1927, in *Postum Cereal Co.* v. *California Fig Nut Co.*, 272 U.S. 693, which has been widely interpreted as precluding certiorari jurisdiction over patent and trademark decisions of the CCPA.

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n5 The present case is the first in which the Government has taken the position that § 1256 confers jurisdiction upon this Court to review patent decisions in the CCPA. Prior to *Glidden Co.* v. *Zdanok*, 370 U.S. 530, the Government was of the view that the Court lacked jurisdiction. See, *e. g.*, the Brief in Opposition in *Dalton* v. *Marzall*, No. 87, O. T. 1951, cert. denied, 342 U.S. 818. After the decision in *Glidden*, discussed *infra*, at 526, the Government conceded the issue was a close one. See, *e. g.*, Brief in Opposition in *In re Gruschwitz*, No. 579, O. T. 1963,

cert. denied, 375 U.S. 967.

n6 We find no warrant for this curious limitation either in the statutory language or in the legislative history of § 1256. Nor do we find persuasive the circumstance that the Commissioner may not appeal adverse decisions of the Board of Appeals. 35 U. S. C. §§ 141, 142, and 145 (1964 ed.). As a member of the Board and the official responsible for selecting the membership of its panels, 35 U. S. C. § 7 (1964 ed.), the Commissioner may be appropriately considered as bound by Board determinations. No such consideration operates to prevent his seeking review of adverse decisions rendered by the CCPA.

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Postum, however, was based upon a statutory scheme materially different from the present one. *Postum* involved a proceeding in the Patent Office to cancel a trademark. The Commissioner of Patents rejected the application. An appeal was taken to the then Court of Appeals for the District of Columbia, which in 1927 exercised the jurisdiction later transferred to the CCPA. Under the statutory arrangement in effect at the time, the judgment of the Court of Appeals was not definitive because it was not an order to the Patent Office determinative of the controversy. A subsequent bill in equity could be brought in the District Court and it was possible that a conflicting adjudication could thus be obtained. On this basis, the Court held that it could not review the decision of the Court of Appeals. It held that the conclusion of the Court of Appeals was an "administrative decision" rather than a "judicial judgment": "merely an instruction to the Commissioner of Patents by a court which is made part of the machinery of the Patent Office for administrative purposes." 272 U.S., at 698-699. Therefore, this Court concluded, the proceeding in the Court of Appeals -- essentially administrative in nature -- was neither case nor controversy within the meaning of Article III of the Constitution. Congress might confer such "administrative" tasks upon the courts of the District of Columbia, wrote Chief Justice Taft, but it could not empower this Court to participate therein.

Congress soon amended the statutory scheme. In March of 1927 it provided that an action in the District Court was to be alternative and not cumulative to appellate review, that it could not be maintained to overcome **[*525]** an adjudication **[**1037]** in the Court of Appeals. n7 In 1929 Congress transferred appellate jurisdiction over the Commissioner's decisions from the Court of Appeals to what had been the Court of Customs Appeals and was now styled the Court of Customs and Patent Appeals. n8 Whereas the Court of Appeals had been empowered to take additional evidence and to substitute its judgment for that of the Commissioner, the CCPA was confined to the record made in the Patent Office. n9 Compare *Federal Communications Comm'n* v. *Pottsville Broadcasting Co.*, 309 U.S. 134, 144-145. Despite these changes, however, *Postum* had acquired a life of its own. It continued to stand in the way of attempts to secure review here of CCPA decisions respecting the Commissioner of Patents. See, *e. g.*, *McBride* v. *Teeple*, 311 U.S. 649, denying certiorari for "want of jurisdiction" on the authority of *Postum*. n10

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n7 Act of March 2, 1927, c. 273, § 11, 44 Stat. 1335, 1336. See *Glidden Co.* v. *Zdanok, supra*, at 572-579; Kurland & Wolfson, Supreme Court Review of the Court of Customs and Patent Appeals, 18 Geo. Wash. L. Rev. 192 (1950). This remains the law. 35 U. S. C. §§ 141, 145.

n8 Act of March 2, 1929, c. 488, 45 Stat. 1475.

n9 See Kurland & Wolfson, *op. cit. supra*, n. 7, at 196.

n10 Apart from *Postum*, until enactment of § 1256 in 1948 there existed no statutory basis for jurisdiction in these cases. See Robertson & Kirkham, Jurisdiction of the Supreme Court of the United States, § 251 (Wolfson & Kurland ed. 1951).

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This **[***75]** was the background against which Congress, in its 1948 codification of statutes pertaining to the judiciary, enacted § 1256, blandly providing in unqualified language for review on certiorari of "cases in the Court of Customs and Patent Appeals." Nothing in the legislative materials relating to the statute, except its language, is of assistance to us in the resolution of the present problem: Did the statutory changes which followed **[*526]** *Postum* mean that a patent decision by the CCPA was a "judicial" determination reviewable by this Court under Article III? And, if so, was § 1256 intended to create such jurisdiction?

Assistance came with the 1958 revision of the Judicial Code. Congress there declared

HN4 the CCPA "a court established under article III . . . ," that is, a constitutional court exercising judicial rather than administrative power. 28 U. S. C. § 211 (1964 ed.). In 1962 this Court addressed itself to the nature and status of the CCPA. *Glidden Co.* v. *Zdanok*, 370 U.S. 530, raised the question whether a judge of the CCPA was an Article III judge, capable of exercising federal judicial power. In answering that question in the affirmative, MR. JUSTICE HARLAN's opinion, for three of the seven Justices participating, expressly left open the question whether § 1256 conferred certiorari jurisdiction over patent and trademark cases decided in the CCPA, 370 U.S., at 578 n. 49. It suggested, however, that *Postum* might be nothing more than a museum piece. The opinion noted that *Postum* "must be taken to be limited to the statutory scheme in existence before" 1929. 370 U.S., at 579. The concurring opinion of MR. JUSTICE CLARK, in which THE CHIEF JUSTICE joined, did not reflect any difference on this point.

[*HR2]** [2]
[*HR3]** [3]
Thus, the decision sought to be reviewed is that of an Article III court. It is "judicial" in character. It is not merely an instruction to the Commissioner or part of the "administrative machinery" of the Patent Office. It is final and binding in the usual sense. n11 **[**1038]** In sum, *Postum* **[*527]** has no vitality in the present setting, and there remains no constitutional bar to our jurisdiction.

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n11 This is not to say that a CCPA determination that an applicant is entitled to apatent precludes a contrary result in a subsequent infringement suit, any more than issuance of a patent by the Patent Office or the decision in an earlier infringement action against a different "infringer" has that effect. See, *e. g., Graham* v. *John Deere Co., ante*, p. 1, at 4. We review decisions of the District Court under 35 U. S. C. § 145 although these are subject to the same measure of readjudication in infringement suits. See *Hoover Co.* v. *Coe*, 325 U.S. 79.

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Having arrived at this conclusion, we have no difficulty in giving full force and effect to the generality of the language in § 1256. It would be entirely arbitrary for us to assume, despite the statutory language, that Congress in 1948 intended to enshrine *Postum* -- dependent as it was upon a statutory scheme fundamentally altered in 1927 and 1929 -- as a hidden exception

to the sweep of § 1256. The contrary is more plausible: that by using broad and unqualified language, Congress intended our certiorari jurisdiction over CCPA cases to be as broad as the Constitution permits.

[*76]**

[*HR5]** [5]
[*HR6]** [6]
[*HR7]** [7]
This conclusion is reinforced by reference to the anomalous consequences which would result were we to adopt a contrary view of § 1256. HN5 Determinations of the Patent Office may be challenged either by appeal to the CCPA or by suit instituted in the United States District Court for the District of Columbia. 35 U. S. C. § 145, 28 U. S. C. § 1542 (1964 ed.). Where the latter route is elected, the decision obtained may be reviewed in the Court of Appeals for the District of Columbia Circuit, and ultimately in this Court upon writ of certiorari. *Hoover Co.* v. Coe, 325 U.S. 79. It would be strange indeed if corresponding certiorari jurisdiction did not exist where the alternative route was elected. Were that so, in the event of conflict between the CCPA and the courts of the District of Columbia, resolution by this Court would be achievable only if the litigants chose to proceed through the latter. Obviously, the orderly administration both of our certiorari jurisdiction and of the patent laws requires that ultimate review be available in this Court, regardless of the route chosen by the litigants.

[*528]

[*HR8]** [8]
[*HR9A]** [9A]
[*HR10A]** [10A]
[*HR11A]** [11A]

We therefore conclude that § 1256 authorizes the grant of certiorari in the present case. We now turn to the merits. n12

[*HR9B]** [9B]
[*HR10B]** [10B]
[*HR11B]** [11B]

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n12 Respondent and the *amicus curiae* take a different view than does the Government of precisely what the issue on the merits is. They argue that the issue of "patentability" is not properly before us, that the issue actually presented is whether the Primary Examiner in the Patent Office has authority under Rule 204 (b) himself to evaluate the sufficiency of affidavits submitted under that Rule. Both the Board of Appeals and the CCPA rejected this view and focused instead on the question of what averments satisfy the statutory requirement that a claimed chemical process be "useful." We agree. First, the issue of "patentability" cannot be foreclosed by the circumstance that the Patent Office -- which, according to counsel for respondent, processes some 1,800 claims and issues 700 patents each week -- has already issued a patent to Ringold and Rosenkranz who asserted in their claim that their process yielded useful products. See note 1, *supra*. Second, there is no basis for the proposition that even where an applicant for an interference presents a claim which on its face is unpatentable,

a complicated and frequently lengthy factual inquiry into priority of invention must inexorably take place. On the contrary, Rule 201 (a), 37 CFR § 1.201 (a), HN6 defines an interference proceeding as one involving "two or more parties claiming substantially the same *patentable* invention and may be instituted as soon as it is determined that common *patentable* subject matter is claimed . . . ." (Emphasis supplied.) See *Application of Rogoff*, 46 C. C. P. A. (Pat.) 733, 739, 261 F.2d 601, 606: "The question as to patentability of claims to an applicant must be determined before any question of interference arises and claims otherwise unpatentable to an applicant cannot be allowed merely in order to set up an interference." See also *Wirkler* v. *Perkins*, 44 C. C. P. A. (Pat.) 1005, 1008, 245 F.2d 502, 504. Cf. *Glass* v. *De Roo*, 44 C. C. P. A. (Pat.) 723, 239 F.2d 402.

The current version of Rule 203 (a), 37 CFR § 1.203 (a), HN7 makes it explicit that the examiner, "before the declaration of interference," must determine the patentability of the claim as to each party. See also Rule 237, 37 CFR § 1.237.

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II.

[1039]**

[*HR12]** [12]

Our starting point is the proposition, neither disputed nor disputable, that HN8 one may patent only that which is **[*529]** "useful." In *Graham* v. *John Deere Co., ante*, p. 1, at 5-10, we have reviewed the history of the requisites of patentability, and it need not be repeated here. Suffice it to say that the concept of utility has maintained a central place in all of our patent legislation, beginning with the first patent law in 1790 n13 and culminating in the present law's **[***77]** provision that

HN9 "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." n14

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n13 See Act of April 10, 1790, c. 7, 1 Stat. 109; Act of Feb. 21, 1793, c. 11, 1 Stat. 318; Act of July 4, 1836, c. 357, 5 Stat. 117; Act of July 8, 1870, c. 230, 16 Stat. 198; Rev. Stat. § 4886 (1874).

n14 35 U. S. C. § 101 (1964 ed.).

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As is so often the case, however, a simple, everyday word can be pregnant with ambiguity when applied to the facts of life. That this is so is demonstrated by the present conflict between the Patent Office and the CCPA over how the test is to be applied to a chemical process which yields an already known product whose utility -- other than as a possible object of scientific inquiry -- has not yet been evidenced. It was not long ago that agency and court seemed of one mind on the question. In *Application of Bremner*, 37 C. C. P. A. (Pat.) 1032, 1034, 182 F.2d 216, 217, the court affirmed rejection by the Patent Office of both process and product claims. It noted that "no use for the products claimed to be developed by the processes had been shown in the specification." It held that "It was never intended that a patent be granted upon a product, or a process producing a product, unless such product be useful." Nor was this new doctrine in the court. See *Thomas* v. *Michael*, 35 C. C. P. A. (Pat.) 1036, 1038-1039, 166 F.2d 944, 946-947.

[*530] The Patent Office has remained steadfast in this view. The CCPA, however, has moved sharply away from *Bremner*. The trend began in *Application of Nelson*, 47 C. C. P. A. (Pat.) 1031, 280 F.2d 172. There, the court reversed the Patent Office's rejection of a claim on a process yielding chemical intermediates "useful to chemists doing research on steroids," despite the absence of evidence that any of the steroids thus ultimately produced were themselves "useful." The trend has accelerated, n15 culminating in the present case where the court held it sufficient that a process produces the result intended and is not "detrimental to the public interest." 52 C. C. P. A. (Pat.), at 745, 333 F.2d, at 238.

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n15 Thus, in *Application of Wilke*, 50 C. C. P. A. (Pat.) 964, 314 F.2d 558, the court reversed a Patent Office denial of a process claim, holding that 35 U. S. C. § 112 (1964 ed.) was satisfied even though the specification recited only the manner in which the process was to be used and not any use for the products thereby yielded. See also *Application of Adams*, 50 C. C. P. A. (Pat.) 1185, 316 F.2d 476.

In *Application of Szwarc*, 50 C. C. P. A. (Pat.) 1571, 319 F.2d 277, the court acknowledged that its view of the law respecting utility of chemical processes had changed since *Bremner*. See generally, Note, The Utility Requirement in the Patent Law, 53 Geo. L. J. 154, 175-181 (1964).

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It is not remarkable that differences arise as to how the test of usefulness is to be applied to chemical processes. Even if we knew precisely what Congress meant in 1790 when it devised the "new **[**1040]** and useful" phraseology and in subsequent re-enactments of the test, we should have difficulty in applying it in the context of contemporary chemistry where research is as comprehensive as man's grasp and where little or nothing is wholly beyond the pale of "utility" -- if that word is given its broadest reach.

[*HR13]** [13]
[*HR14A]** [14A]
Respondent does not -- at least in the first instance -- rest upon the extreme proposition, advanced by the court below, that a novel chemical process is patentable so long **[*531]** as it yields the intended product n16 **[***78]** and so long as the product is not itself "detrimental." Nor does he commit the outcome of his claim to the slightly more conventional proposition that any process is "useful" within the meaning of § 101 if it produces a compound whose potential usefulness is under investigation by serious scientific researchers, although he urges this position, too, as an alternative basis for affirming the decision of the CCPA. Rather, he begins with the much more orthodox argument that his process has a specific utility which would entitle him to a declaration of interference even under the Patent Office's reading of § 101. The claim is that the supporting affidavits filed pursuant to Rule 204 (b), by reference to Ringold's 1956 article, reveal that an adjacent homologue of the steroid yielded by his process has been demonstrated to have tumor-inhibiting effects in mice, and that this discloses the requisite utility. We do not accept any of these theories as an adequate basis for overriding the determination of the Patent Office that the "utility" requirement has not been met.

[*HR14B]** [14B]

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n16 Respondent couches the issue in terms of whether the process yields a"known" product. We fail to see the relevance of the fact that the product is "known," save to the extent that references to a compound in scientific literature suggest that it might be a subject of interest and possible investigation.

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[*HR15]** [15]
Even on the assumption that the process would be patentable were respondent to show that the steroid produced had a tumor-inhibiting effect in mice, n17 we would **[*532]** not overrule the Patent Office finding that respondent has not made such a showing. The Patent Office held that, despite the reference to the adjacent homologue, respondent's papers did not disclose a sufficient likelihood that the steroid yielded by his process would have similar tumor-inhibiting characteristics. Indeed, respondent himself recognized that the presumption that adjacent homologues have the same utility n18 has been challenged in the steroid field because of "a greater known unpredictability of compounds in that field." n19 In these circumstances and in this technical area, we would not overturn the finding of the Primary Examiner, affirmed by the Board of Appeals and not challenged by the CCPA.

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n17 In light of our disposition of the case, we express no view as to the patentability of a process whose sole demonstrated utility is to yield a product shown to inhibit the growth of tumors in laboratory animals. See *Application of Hitchings*, 52 C. C. P. A. (Pat.) 1141, 342 F.2d 80; *Application of Bergel*, 48 C. C. P. A. (Pat.) 1102, 292 F.2d 955; cf. *Application of Dodson*, 48 C. C. P. A. (Pat.) 1125, 292 F.2d 943; *Application of Krimmel*, 48 C. C. P. A. (Pat.) 1116, 292 F.2d 948. For a Patent Office view, see Marcus, The Patent Office and Pharmaceutical Invention, 47 J. Pat. Off. Soc. 669, 673-676 (1965).

n18 See n. 3, *supra*.

n19 See respondent's letter requesting amendment, dated July 21, 1960, Record, pp. 20-23.

See also *Application of Adams*, 50 C. C. P. A. (Pat.) 1185, 1190, 316 F.2d 476, 479-480 (concurring-dissenting opinion). In the present case, the Board of Appeals found support in the Ringold article itself for the view that "minor changes in the structure of a steroid may produce profound changes in its biological activity." Record, p. 52.

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The second and third points of respondent's argument present issues of much importance. Is a chemical process "useful" within the meaning of § 101 either (1) because it works -- *i. e.*, produces the intended product? or (2) because **[**1041]** the compound yielded belongs to a class of compounds now the subject of serious scientific investigation? These contentions present the basic problem for our adjudication. **[***79]** Since we find no specific assistance in the legislative materials underlying § 101, we are remitted to an analysis of the problem in light of the general intent of Congress, the purposes of the patent system, and the implications of a decision one way or the other.

In support of his plea that we attenuate the requirement of "utility," respondent relies upon Justice Story's **[*533]** well-known statement that a "useful" invention is one "which may be applied to a beneficial use in society, in contradistinction to an invention injurious to the morals, health, or good order of society, or frivolous and insignificant" n20 -- and upon the assertion that to do so would encourage inventors of new processes to publicize the event for the benefit of the entire scientific community, thus widening the search for uses and increasing the fund of scientific knowledge. Justice Story's language sheds little light on our subject. Narrowly read, it does no more than compel us to decide whether the invention in question is "frivolous and insignificant" -- a query no easier of application than the one built into the statute. Read more broadly, so as to allow the patenting of any invention not positively harmful to society, it places such a special meaning on the word "useful" that we cannot accept it in the absence of evidence that Congress so intended. There are, after all, many things in this world which may not be considered "useful" but which, nevertheless, are totally without a capacity for harm.

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n20 Note on the Patent Laws, 3 Wheat. App. 13, 24. See also Justice Story's decisions on circuit in *Lowell* v. *Lewis*, 15 Fed. Cas. 1018 (No. 8568) (C. C. D. Mass.), and *Bedford* v. *Hunt*, 3 Fed. Cas. 37 (No. 1217) (C. C. D. Mass.).

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It is true, of course, that one of the purposes of the patent system is to encourage dissemination of information concerning discoveries and inventions. n21 And it may be that inability to patent a process to some extent discourages disclosure and leads to greater secrecy than would otherwise be the case. The inventor of the process, or the corporate organization by which he is employed, has some incentive to keep the invention **[*534]** secret while uses for the product are searched out. However, in light of the highly developed art of drafting patent claims so that they disclose as little useful information as possible -- while broadening the scope of the claim as widely as possible -- the argument based upon the virtue of disclosure must be warily evaluated. Moreover, the pressure for secrecy is easily exaggerated, for if the inventor of a process cannot himself ascertain a "use" for that which his process yields, he has every incentive to make his invention known to those able to do so. Finally, how likely is disclosure of a patented process to spur research by others into the uses to which the product may be put? To the extent that the patentee has power to enforce his patent, there is little incentive for others to undertake a search for uses.

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n21 "As a reward for inventions and to encourage their disclosure, the United States offers a seventeen-year monopoly to an inventor who refrains from keeping his invention a trade secret." *Universal Oil Prods. Co.* v. Globe Oil & Ref. Co., 322 U.S. 471, 484.

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[*HR17]** [17]
[*HR18]** [18]
Whatever weight is attached to the value of encouraging disclosure and of inhibiting secrecy, we believe a more compelling consideration is that a process patent in the chemical field, which has not been developed and pointed to the degree of specific utility, creates a **[***80]** monopoly of knowledge which should be granted only if clearly commanded by the statute. Until the process claim has been reduced to production of a product **[**1042]** shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation. It may engross a vast, unknown, and perhaps unknowable area. Such a patent may confer power to block off whole areas of scientific development, n22 without compensating benefit to the public. The basic *quid pro quo* contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. HN10 Unless and until a process is refined and developed to this point -- where specific benefit **[*535]** exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field.

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n22 See *Monsanto Chemical Co.* v. Coe, 79 U. S. App. D. C. 155, 158-161, 145 F.2d 18, 21-24.

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These arguments for and against the patentability of a process which either has no known use or is useful only in the sense that it may be an object of scientific research would apply equally to the patenting of the product produced by the process. Respondent appears to concede that with respect to a product, as opposed to a process, Congress has struck the balance on the side of nonpatentability unless "utility" is shown. Indeed, the decisions of the CCPA are in accord with the view that a product may not be patented absent a showing of utility greater than any adduced in the present case. n23 We find absolutely no warrant for the proposition that although Congress intended that no patent be granted on a chemical compound whose sole "utility" consists of its potential role as an object of use-testing, a different set of rules was meant to apply to the process which yielded the unpatentable product. n24 That proposition seems to us little more than an attempt to evade the impact of the rules which concededly govern patentability of the product itself.

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n23 See, *e. g.*, the decision below, 52 C. C. P. A. (Pat.), at 744, 333 F.2d, at 237. See also

Application of Bergel, 48 C. C. P. A. (Pat.), at 1105, 292 F.2d, at 958. Cf. *Application of Nelson*, 47 C. C. P. A. (Pat.), at 1043-1044, 280 F.2d, at 180-181; *Application of Folkers*, 52 C. C. P. A. (Pat.) 1269, 344 F.2d 970.

n24 The committee reports which preceded enactment of the 1952 revision of the patent laws disclose no intention to create such a dichotomy, and in fact provide some evidence that the contrary was assumed. Sen. Rep. No. 1979, Committee on the Judiciary, 82d Cong., 2d Sess., 5, 17; H. R. Rep. No. 1923, Committee on the Judiciary, 82d Cong., 2d Sess., 6, 17. Cf. Hoxie, A Patent Attorney's View, 47 J. Pat. Off. Soc. 630, 636 (1965).

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[*HR20]** [20]
This is not to say that we mean to disparage the importance of contributions to the fund of scientific information **[*536]** short of the invention of something "useful," or that we are blind to the prospect that what now seems without "use" may tomorrow command the grateful attention of the public. But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. HN11 "[A] patent system must be related to the world of commerce rather than to the realm of philosophy. . . ." n25

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n25 *Application of Ruschig*, 52 C. C. P. A. (Pat.) 1238, 1245, 343 F.2d 965, 970 (Rich, J.). See also, *Katz v. Horni Signal Mfg. Corp.*, 145 F.2d 961 (C. A. 2d Cir.).

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The judgment of the CCPA is

Reversed.

MR. JUSTICE DOUGLAS, while acquiescing in Part I of the Court's **[***81]** opinion, dissents on the merits of the controversy for substantially the reasons stated by MR. JUSTICE HARLAN.

CONCURBY: HARLAN (In Part)

DISSENTBY: HARLAN (In Part)

DISSENT: MR. JUSTICE HARLAN, concurring in part and dissenting in part.

While I join the Court's opinion on the issue of certiorari jurisdiction, I cannot agree with its resolution of the important question of patentability.

Respondent has contended that a workable chemical process, which is both new and sufficiently nonobvious to satisfy **[**1043]** the patent statute, is by its existence alone a contribution to chemistry and "useful" as the statute employs that term. n1 Certainly this reading of "useful" in the statute is within the scope of the constitutional grant, which states only that "to promote the Progress of Science and useful Arts," the exclusive right to "Writings and Discoveries" may be secured for limited times to those who produce them. Art. I, § 8. Yet

the patent statute is somewhat differently worded and is on **[*537]** its face open both to respondent's construction and to the contrary reading given it by the Court. In the absence of legislative history on this issue, we are thrown back on policy and practice. Because I believe that the Court's policy arguments are not convincing and that past practice favors the respondent, I would reject the narrow definition of "useful" and uphold the judgment of the Court of Customs and Patent Appeals (hereafter CCPA).

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n1 The statute in pertinent part is set out in the Court's opinion, p. 529, *ante*.

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The Court's opinion sets out about half a dozen reasons in support of its interpretation. Several of these arguments seem to me to have almost no force. For instance, it is suggested that "until the process claim has been reduced to production of a product shown to be useful, the metes and bounds of that monopoly are not capable of precise delineation" (p. 534, *ante*) and "it may engross a vast, unknown, and perhaps unknowable area" (p. 534, *ante*). I fail to see the relevance of these assertions; process claims are not disallowed because the products they produce may be of "vast" importance nor, in any event, does advance knowledge of a specific product use provide much safeguard on this score or fix "metes and bounds" precisely since a hundred more uses may be found after a patent is granted and greatly enhance its value.

The further argument that an established product use is part of "the basic *quid pro quo*" (p. 534, *ante*) for the patent or is the requisite "successful conclusion" (p. 536, *ante*) of the inventor's search appears to beg the very question whether the process is "useful" simply because it facilitates further research into possible product uses. The same infirmity seems to inhere in the Court's argument that chemical products lacking immediate utility cannot be distinguished for present purposes from the processes which create them, that respondent appears to concede and the CCPA holds that **[*538]** the products are nonpatentable, and that therefore the processes are nonpatentable. Assuming that the two classes cannot be distinguished, a point not adequately considered in the briefs, and assuming further that the CCPA has firmly held such products nonpatentable, n2 **[***82]** this permits us to conclude only that the CCPA is wrong either as to the products or as to the processes and affords no basis for deciding whether both or neither should be patentable absent a specific product use.

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n2 Any concession by respondent would hardly be controlling on an issue of this general importance, but I am less clear than the Court that such a concession exists. See, *e. g.*, Brief for Respondent, p. 53. As to the CCPA, it is quite true that the court purports in the very case under review and in others to distinguish product patents, although its actual practice may be somewhat less firm. See *Application of Adams*, 50 C. C. P. A. (Pat.) 1185, 316 F.2d 476, *Application of Nelson*, 47 C. C. P. A. (Pat.) 1031, 280 F.2d 172.

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More to the point, I think, are the Court's remaining, prudential arguments against patentability: namely, that disclosure induced by allowing a patent is partly undercut by patent-application drafting techniques, that disclosure may occur without granting a patent, and that a patent will discourage others from inventing uses for the product. How far opaque drafting may lessen the public benefits resulting from the issuance of a patent is not shown by any evidence in **[**1044]** this case but, more important, the argument operates against all patents and gives no reason for singling out the class involved here. The thought that these inventions may be more likely than most to be disclosed even if patents are not allowed may

have more force; but while empirical study of the industry might reveal that chemical researchers would behave in this fashion, the abstractly logical choice for them seems to me to maintain secrecy until a product use can be discovered. As to discouraging the search by **[*539]** others for product uses, there is no doubt this risk exists but the price paid for any patent is that research on other uses or improvements may be hampered because the original patentee will reap much of the reward. From the standpoint of the public interest the Constitution seems to have resolved that choice in favor of patentability.

What I find most troubling about the result reached by the Court is the impact it may have on chemical research. Chemistry is a highly interrelated field and a tangible benefit for society may be the outcome of a number of different discoveries, one discovery building upon the next. To encourage one chemist or research facility to invent and disseminate new processes and products may be vital to progress, although the product or process be without "utility" as the Court defines the term, because that discovery permits someone else to take a further but perhaps less difficult step leading to a commercially useful item. In my view, our awareness in this age of the importance of achieving and publicizing basic research should lead this Court to resolve uncertainties in its favor and uphold the respondent's position in this case.

This position is strengthened, I think, by what appears to have been the practice of the Patent Office during most of this century. While available proof is not conclusive, the commentators seem to be in agreement that until *Application of Bremner*, 37 C. C. P. A. (Pat.) 1032, 182 F.2d 216, in 1950, chemical patent applications were commonly granted although no resulting end use was stated or the statement was in extremely broad terms. n3 Taking **[***83]** this to be true, *Bremner* represented **[*540]** a deviation from established practice which the CCPA has now sought to remedy in part only to find that the Patent Office does not want to return to the beaten track. If usefulness was typically regarded as inherent during a long and prolific period of chemical research and development in this country, surely this is added reason why the Court's result should not be adopted until Congress expressly mandates it, presumably on the basis of empirical data which this Court does not possess.

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n3 See, *e. g.*, the statement of a Patent Office Examiner-in-Chief:

"Until recently it was also rather common to get patents on chemical compounds in cases where no use was indicated for the claimed compounds or in which a very broad indication or suggestion as to use was included in the application. [*Bremner* and another later ruling] . . . have put an end to this practice." Wolffe, Adequacy of Disclosure as Regards Specific Embodiment and Use of Invention, 41 J. Pat. Off. Soc. 61, 66 (1959). The Government's brief in this case is in accord: "It was apparently assumed by the Patent Office [prior to 1950] . . . that chemical compounds were necessarily useful . . . and that specific inquiry beyond the success of the process was therefore unnecessary . . . ." Brief for the Commissioner, p. 25. See also Cohen & Schwartz, Do Chemical Intermediates Have Patentable Utility? 29 Geo. Wash. L. Rev. 87, 91 (1960); Note, 53 Geo. L. J. 154, 183 (1964); 14 Am. U. L. Rev. 78 (1964).

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Fully recognizing that there is ample room for disagreement on this problem when, as here, it is reviewed in the abstract, I believe the decision below should be affirmed.

*753 F.2d 1040, *; 1985 U.S. App. LEXIS 14694, **;*
224 U.S.P.Q. (BNA) 739

PETER E. CROSS, ET AL., Appellants v. KINJI IIZUKA, ET AL., Appellees

No. 84-1111

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

753 F.2d 1040; 1985 U.S. App. LEXIS 14694; 224 U.S.P.Q. (BNA) 739

January 28, 1985

PRIOR HISTORY: [1]**

Appealed from United States Patent & Trademark Office.

CASE SUMMARY

PROCEDURAL POSTURE: Appellant sought review of the decision of the United States Patent and Trademark Office Board of Patent Interferences awarding priority on a count to appellee in determination of applications filed by both parties under 35 U.S.C.S. § 119.

OVERVIEW: Appellant and appellee submitted patent applications to the Board for priority of a pharmacological compound, each moving to be accorded a foreign priority application under 35 U.S.C.S. § 119 and asserting the other's application did not comply with the disclosure requirements of 35 U.S.C.S. § 112. Because appellee filed the priority application first, appellee was declared the senior party and the Board held appellee's application contained an adequate how-to-use disclosure for the practical utility stated therein. Appellant sought review. The court held that where the Board was charged with the factual determination of utility and found the specifications of appellee's application disclosed the compound's utility and where credible evidence to support that factual determination existed, the determination would be upheld. As appellant bore the burden of proof to show that the Board erred in finding appellee's priority application adequately disclosed a practical utility and failed to do so, the Board's determination that appellee's application had a practical utility was upheld.

OUTCOME: The court affirmed the judgment.

CORE TERMS: compound, imidazole, thromboxane, pharmacological, practical utility, synthetase, vitro, derivative, phantom, vivo, microsome, inhibitory, disclosure, platelet, invention, methylimidazole, testing, reduction, bovine, dosage, patent, how-to-use, aggregation, inhibition, specification, correlation, skilled, skill, therapeutic, concentration

LexisNexis(R) Headnotes ◆ Hide Headnotes

Patent Law > Utility Requirement > Proof of Utility

HN1 An invention cannot be considered useful, in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN2 Where a constructive reduction to practice is involved, as contrasted to an actual reduction to practice, a practical utility for the invention is determined by reference to, and a factual analysis of, the disclosures of the application. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN3 Evidence of any utility is sufficient when the count does not recite any particular utility. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN4 A consideration in the determination of whether a patent should be granted is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point -- where specific benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field. More Like This Headnote

Patent Law > Utility Requirement > Chemical Compounds

HN5 Knowledge of the pharmacological activity of any compound is obviously beneficial to the public and adequate proof of any such utility constitutes a showing of practical utility. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

HN6 Where a count contains no limitation related to utility, evidence establishing a substantial utility for any purpose is sufficient to show a reduction to practice. More Like This Headnote

Patent Law > Utility Requirement > Chemical Compounds

HN7 Every utility question arising in an interference, in the final analysis, must be decided on the basis of its own unique factual circumstances. Relevant evidence must be judged as a whole for its persuasiveness in determining whether the suggested use for the compound of the count is a practical utility. More Like This Headnote

Patent Law > Utility Requirement > Chemical Compounds

HN8 A particular pharmacological activity identified with prior art compounds may have probative value as to the fact that the compound of the count possesses this particular pharmacological activity where there is a structural similarity between the prior art compounds and the compound of the count. More Like This Headnote

Patent Law > Utility Requirement > Proof of Utility

Patent Law > Utility Requirement > Chemical Compounds

HN9 Adequate proof of any pharmacological activity constitutes a showing of practical utility. More Like This Headnote

COUNSEL: Rudolf E. Hutz, Connolly, Bove, Lodge & Hutz, of Wilmington, Delaware, argued for Appellants. With him on the brief was Thomas M. Meshbesher.

Peter D. Olexy, Sughrue, Mion, Zinn, MacPeak, & Seas, of Washington, District of Columbia, argued for Appellees. With him on the brief was Thomas J. MacPeak.

JUDGES: Kashiwa, Bennett, and Bissell, Circuit Judges.

OPINIONBY: KASHIWA

OPINION: [*1041] KASHIWA, Circuit Judge.

This appeal is from the decision of the United States Patent and Trademark Office (PTO) Board of Patent Interferences (Board) awarding priority on the single phantom count to Iizuka, *et al.* (Iizuka), the senior party. We affirm.

Background

Interference No. 100,650 was declared on 20 April 1981 between application serial No. 68,365, for "Imidazole Derivatives," filed by Iizuka on 21 August 1979 and application serial No. 95,755, for "N- (Phenoxyalkyl) Imidazoles as Selective Inhibitors of the Thromboxane Synthetase Enzyme and Pharmaceutical Compositions **[*1042]** Thereof," filed by Cross, *et al.* (Cross) on 19 November 1979. The single phantom count of the interference is directed to imidazole **[**2]** derivative compounds and reads as follows:

> A compound selected from the group consisting of an imidazole derivative of the formula
>
> [SEE ILLUSTRATION IN ORIGINAL]
> wherein R is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms, each of A[1] or A[2], which may be the same or different, are alkylene having 1 to 8 carbon atoms, m is 0 or 1, X is oxygen or sulfur, and each of R[1] or R[2], which may be the same or different, is a hydrogen atom or an alkyl group having 1 to 6 carbon atoms; R[3] is H, C[1]-C[4] alkyl, C[1]-C[4] alkoxy or halogen; and the pharmaceutically acceptable salts thereof. n1

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n1 We note a discrepancy, shown underlined in the above count, between the phantom count as set forth by the primary examiner and that reported by the Board in its decision. The phantom count set forth herein is the one propounded by the primary examiner. However, as will become apparent from the ensuing discussion, the substance of the phantom count is not crucial to resolution of the issues presented by this case.

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The applications of Cross and Iizuka both disclose inventions directed to imidazole derivative compounds which inhibit the synthesis of thromboxane synthetase, an enzyme which leads to the formation of thromboxane A[2] (TXA[2]), n2 a highly unstable, biologically active compound which is converted to stable thromboxane B[2] by the addition of water. Thromboxane A[2], as of the time period during which the applications were filed, was postulated to be a causal factor in platelet aggregation. n3 Platelet aggregation is associated with several deleterious conditions in mammalia, including humans, such as platelet thrombosis, pulmonary vasoconstriction or vasospasm, inflammation, hypertension, and collagen-induced thrombosis.

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n2 The formation of TXA[2] in an arachidonic acid challenge is a sequential process initiated by the conversion of arachidonic acid to prostaglandin PGG[2] by the action of cyclooxygenase, which adds oxygen to the acid. Peroxidase converts the prostaglandin PGG[2] to prostaglandin PGH[2], which in turn is converted by thromboxane synthetase to TXA[2]. **[**4]**

n3 Iizuka's position is that, as of the "critical date" of his application, TXA[2] was widely accepted in the art as causing platelet aggregation. Cross' position is that, as of the "critical

date," platelet aggregation was believed to be nonspecific, i.e., platelet aggregation *may* occur in the presence of thromboxane synthetase, but thromboxane synthetase is not necessary for platelet aggregation. We note in retrospect that THE MERCK INDEX 1345-46 (10th ed. 1983) describes TXA[2] as inducing irreversible platelet aggregation. More to the point, however, this court has noted that it is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests, nor is the inventor's theory or belief as to how his invention works a necessary element in the specification to satisfy the enablement requirement of 35 U.S.C. § 112. *Fromson v. Advance Offset Plate, Inc.*, 720 F.2d 1565, 1570, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed. Cir. 1983).

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Pursuant to 37 C.F.R. § 1.231(a)(4) each party moved to be accorded the benefit of the **[**5]** foreign priority application under 35 U.S.C. § 119, Cross claiming priority based upon a British application filed 13 December 1978, and Iizuka claiming priority based upon a Japanese application filed 21 August 1978. Each party opposed the motion of the other party, each party contending that the other party's foreign priority application did not comply with the disclosure requirements of 35 U.S.C. § 112.

The primary examiner granted each party's motion, noting that the utility alleged in each application was of a pharmacological nature, i.e., the inhibition of thromboxane synthetase, and that inasmuch as the single phantom count of the interference was directed to a compound, it was not necessary that utility be established by tests and dosages with respect to human beings. The examiner found that one of ordinary skill in the art would know how to use the imidazole derivatives, i.e., be able to determine specific dosages, for biological purposes. Based upon the filing dates of **[*1043]** the foreign priority applications, n4 Iizuka was declared the senior party and a show cause order was issued against Cross.

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n4 Each party relies on the filing date of its foreign priority application to establish a constructive reduction to practice, the earliest date of invention to which each party is entitled under the patent laws of the United States. *Kawai v. Metlesics*, 480 F.2d 880, 885-86, 178 U.S.P.Q. (BNA) 158, 162 (CCPA 1973).

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Cross requested a final hearing on the issue of the sufficiency of the Japanese priority application of Iizuka, and moved for a testimony period to present evidence on this issue. A testimony period was granted over the opposition of Iizuka, and Cross took the testimony of his expert witness, Dr. Smith, and Iizuka took the testimony of his expert witness, Dr. Ramwell and also proffered several exhibits pursuant to 37 C.F.R. § 1.282. All testimony and exhibits related to the sufficiency of Iizuka's Japanese priority application, i.e., whether it complied with the disclosure requirements of 35 U.S.C. § 112.

Decision of the Board

The Board noted that the sole issue before it was whether Iizuka was entitled to the benefit of his Japanese priority application. n5 Relying on *In re Bundy*, 642 F.2d 430, 209 U.S.P.Q. (BNA) 48 (CCPA 1981), and *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (CCPA 1980), the Board held that tests evidencing pharmacological activity may manifest a practical utility even though they may not establish a specific therapeutic use. The Board found that the Japanese priority application disclosed pharmacological activity in the similar **[**7]** activity of the imidazole derivatives of the count to imidazole and 1-methylimidazole, which possess an inhibitory action for thromboxane synthetase, and that practical utility was disclosed in the strong inhibitory action for thromboxane synthetase from human or bovine platelet microsomes,

i.e., an *in vitro* utility. n6

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n5 More specifically, the issue before the Board was whether the Japanese priority application complied with the how-to-use requirement of 35 U.S.C. § 112. Section 112 of Title 35 provides, in pertinent part, that:

> The specification shall contain a written description of the invention, of the manner and process of making and *using* it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and *use* the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention. (Emphasis added.)

Should Iizuka's Japanese priority application be found nonenabling with respect to the how-to-use requirement of § 112, or otherwise found deficient under the patent laws of the United States, priority would be awarded to Cross based upon his unchallenged entitlement to the benefit of his British application. **[**8]**

n6 Generally, *in vitro* refers to an environment outside of a living organism, usually an artificial environment such as a test tube or culture. In contradistinction, *in vivo* generally refers to an environment within a living organism, such as a plant or animal, or it may refer to a particular portion of an organ external to the living organism, e.g., rat aortic loop.

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The Board further found that the Japanese priority application disclosed "how-to-use" knowledge directed to the practical utility in a microsome system, and that microsome assays were admittedly known in the art. A skilled worker could determine the relative strength of the imidazole compounds of the count vis-a-vis the known parent imidazole and 1-methylimidazole compounds for use in the microsome assay milieu. Knowledge of the pharmacological activities of compounds is beneficial to the medical profession, and requiring Iizuka to have disclosed *in vivo* dosages in the Japanese priority application would delay and frustrate researchers by failing to provide an incentive for early public disclosure of such compounds, **[**9]** thereby failing to further the public interest.

Accordingly, the Board held that the Japanese priority application contained an adequate how-to-use disclosure for the practical utility stated therein.

Issues

Whether the Board erred in finding that the utility disclosed in the Japanese priority application is sufficient to meet the practical utility requirement of 35 U.S.C. § 101.

[*1044] Whether the Board erred in finding that the Japanese priority application contained sufficient disclosure to satisfy the enablement, i.e., how-to-use, requirement of 35 U.S.C. § 112. n7

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n7 Utility is a fact question. *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 956, 220 U.S.P.Q. (BNA) 592, 596 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835, 105 S. Ct. 127, 83 L. Ed. 2d 69, 225 U.S.P.Q. (BNA) 232 (1984). Enablement under § 112, paragraph 1, i.e., the how-to-use requirement, is a question of law. *Id.* at 960 n.6, 220 U.S.P.Q. (BNA) at 599 n.6.

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OPINION

Proper resolution of the issues before this **[**10]** court necessitates that we address, *seriatim*, the following questions: (1) What utility is disclosed by the Japanese priority application? (2) Does this stated utility comply with the "practical utility" requirement of 35 U.S.C. § 101, as delimited by prior decisions of the judiciary? n8 (3) Does the Japanese priority application contain sufficient disclosure to meet the how-to-use requirement of § 112 with respect to the stated utility?

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n8 While questions one and two are closely connected, a thorough analysis of the utility issue requires first, a determination as to what utility is disclosed, i.e., the stated utility, for the invention claimed in the application. Only after the stated utility has been determined, can a proper analysis be undertaken to determine if the stated utility complies with the "practical utility" requirement of § 101. As noted above, these questions regarding utility are factual in nature, *see supra* note 7, and are to be determined in the first instance by the PTO, the agency with the expertise in this regard.

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It is axiomatic that HN1 an invention cannot be considered "useful", in the sense that a patent can be granted on it, unless substantial or practical utility for the invention has been discovered and disclosed where such utility would not be obvious. *Brenner v. Manson*, 383 U.S. 519, 16 L. Ed. 2d 69, 86 S. Ct. 1033, 148 U.S.P.Q. (BNA) 689 (1966). HN2 Where a constructive reduction to practice is involved, as contrasted to an actual reduction to practice, a practical utility for the invention is determined by reference to, and a factual analysis of, the disclosures of the application. *Kawai v. Metlesics*, 480 F.2d 880, 178 U.S.P.Q. (BNA) 158 (CCPA 1973).

1. Japanese Priority Application

The Board factually analyzed the Japanese priority application and found that the only effective disclosure relating to a stated utility for the imidazole derivative compounds of the phantom count was the following:

> [The compounds disclosed] are useful for treatment of inflammation, thrombus, hypertension, cerebral apoplexy, asthma, etc.
>
> Up to this time, it is a known fact that imidazole and 1-methylimidazole possess an inhibitory action for thromboxane synthetase and inhibit a biosynthesis **[**12]** of thromboxane A[2]. (*Prostaglandins*, Vol. 13, pages 611-, *1977*). However, since their inhibitory effect is not satisfactory one, these compounds have not been put to practical use yet as therapeutical medicines for diseases caused by thromboxane A[2], such as inflammation, hypertension,

thrombus, cerebral apoplexy, asthma, etc.

To develop some compounds possessing a strong inhibitory action for biosynthesis of thromboxane A[2], the present inventors devoted themselves to study for various imidazole derivatives, and as a result, found that the compounds [of this invention] possess a strong inhibitory action for thromboxane synthetase from human or bovine platelet microsomes and are extremely useful as therapeutically active agents for diseases caused by thromboxane A[2], for example, inflammation, hypertension, thrombus, cerebral apoplexy, asthma, etc., and thus we proposed this invention based upon those findings.

* * *

The imidazole derivatives . . . of this invention are novel compounds which are not described in literature, and which possess a strong inhibitory action for thromboxane synthetase from human or bovine platelet microsomes, and which **[*1045] [**13]** exhibit a strong inhibitory action for biosynthesis of thromboxane A[2] in mammalia including human. In general, a satisfactory inhibitory effect is found at a level of molar concentrations of 2.5 x 10<-8>, for example, 2-[p-(1-imidazolylmethyl) phenoxy]-acetic acid hydrochloride produce the about 50% inhibitory effect at the molar concentrations of 2.5 x 10<-8>. Accordingly, the imidazole derivatives of this invention are extremely useful as therapeutical medicines for diseases caused by thromboxane A[2], such as inflammation, hypertension, thrombus, cerebral apoplexy, asthma, etc.

The Board found that these pertinent sections of the Japanese priority application disclosed some activity or utility, namely that the imidazole derivative compounds of the count possess a strong inhibitory action for thromboxane synthetase in human or bovine platelet microsomes. Cross' position is that the stated purpose or *sole* contemplated utility of the invention of Iizuka is to provide a novel class of compounds which provide "practical use" as "therapeutical medicines for diseases caused by thromboxane A[2]," and therefore the Board erred in its finding as to the stated utility **[**14]** of the Japanese priority application.

While recognizing that *Kawai* constrains an applicant to entitlement to the benefit of only what is disclosed in the foreign priority application and no more, we also recognize that foreign priority applications, as subsequently filed in the PTO, typically have a style and format dissimilar to the arrangement of application elements suggested by 37 C.F.R. § 1.77. In part this arises because of differences in filing requirements in foreign patent offices, and in part because of the awkwardness resulting from direct literal translations from a foreign language to English. Thus, while the factual determination of the stated utility in an application prepared in the United States may be relatively straightforward, n9 the factual analysis of a foreign priority application to determine the utility disclosed therein may be more laborious and open to varying interpretations.

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n9 In applications prepared in the United States by experienced patent drafters, the drafter of the application typically sets forth objectives for the invention in the "Summary of the Invention" section of the application. These objectives will normally be consonant with the utility disclosed for the invention. As this court has noted, "when a properly claimed invention meets at least one stated objective, utility under § 101 is clearly shown." *Raytheon Co. v. Roper Corp.*, 724 F.2d 951, 958, 220 U.S.P.Q. (BNA) 592, 598 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835,

105 S. Ct. 127, 83 L. Ed. 2d 69 (1984).

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The weakness of Cross' position is that a fair reading of the pertinent sections of the Japanese priority application, as set forth above, discloses utility for the imidazole derivative compounds of the phantom count both as an inhibiting agent for thromboxane synthetase in human or bovine platelet microsomes, as found by the Board, and as therapeutically active agents preventing the biosynthesis of thromboxane A[2], thereby functioning as a medicine preventing deleterious conditions caused by thromboxane A[2], as contended by Cross.

HN3 Evidence of any utility is sufficient when the count does not recite any particular utility. *Nelson v. Bowler*, 626 F.2d 853, 856, 206 U.S.P.Q. (BNA) 881, 883 (CCPA 1980). *See also* *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 181 U.S.P.Q. (BNA) 453 (CCPA 1974); *Knapp v. Anderson*, 477 F.2d 588, 177 U.S.P.Q. (BNA) 688 (CCPA 1973); *Blicke v. Treves*, 44 C.C.P.A. 753, 241 F.2d 718, 112 U.S.P.Q. (BNA) 472 (CCPA 1957). Here the Board, which is charged with the factual determination of utility, n10 has found that the specification of the Japanese priority application disclosed *a* utility for the imidazole derivative compounds of the phantom **[**16]** count in the inhibition of thromboxane **[*1046]** synthetase in human or bovine platelet microsomes. Inasmuch as the Board is charged with making this factual determination when the issue is raised, inasmuch as they have so done in the instant case, and inasmuch as there is credible evidence to support this factual determination, we are not prepared to say that the Board erred in its finding as to the stated utility disclosed in the Japanese priority application.

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n10 Under the facts of the instant case, utility and enablement questions are ancillary to priority. In the interference proceeding, Cross raised the issue as to whether the Japanese priority application contained sufficient disclosure to satisfy § 112. As noted above, *see supra* note 5, if Cross prevails on this issue the Japanese priority application would be removed as the basis for awarding priority to Iizuka. *See generally* 37 C.F.R. §§ 1.225,.231,.258.

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2. Practical Utility

As noted in the preceding part of this opinion, Cross **[**17]** has contended that the Board erred in its finding as to the utility disclosed in the Japanese priority application. This argument may be viewed in a different perspective, we believe, which is that the stated utility in the Japanese priority application, as found by the Board -- the inhibition of thromboxane synthetase in human or bovine platelet microsomes n11 -- is not sufficiently correlated to a pharmacological activity n12 to be a practical utility. In other words, Cross may be arguing that the minimum acceptable level of utility disclosed in an application claiming a compound having pharmacological activity must be directed to an *in vivo* utility in order to comply with the practical utility requirement of § 101.

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n11 A platelet microsome is an *in vitro* milieu consisting of blood platelets, the small, colorless corpuscles in the blood of all mammals, and other finely granular elements of protoplasm, such as ribosomes, fragmented endoplasmic reticula and mitochondrial christae.

n12 Generally, pharmacological activity refers to the properties and reactions of drugs, especially with relation to their therapeutic value.

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The starting point for a practical utility analysis is *Brenner v. Manson*, 383 U.S. 519, 16 L. Ed. 2d 69, 86 S. Ct. 1033, 148 U.S.P.Q. (BNA) 689 (1966). The Court in *Brenner* noted that "a simple, everyday word ["useful," as found in 35 U.S.C. § 101] can be pregnant with ambiguity when applied to the facts of life." *Id.* at 529, 148 U.S.P.Q. (BNA) at 693. HN4 While noting that "one of the purposes of the patent system is to encourage dissemination of information concerning discoveries and inventions," *id.* at 533, 148 U.S.P.Q. (BNA) at 695, the Court found that a more compelling consideration in the determination of whether a patent should be granted "is the benefit derived by the public from an invention with substantial utility. Unless and until a process is refined and developed to this point -- where specific benefit exists in currently available form -- there is insufficient justification for permitting an applicant to engross what may prove to be a broad field." *Id.* at 534-35, 148 U.S.P.Q. (BNA) at 695. While we recognize that this case concerned a compound derived from a chemical process, we believe *Brenner* provides broad guidelines which are helpful in **[**19]** ascertaining what constitutes practical utility for compounds having a pharmacological effect.

HN5 In *Nelson v. Bowler*, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (1980), our predecessor court, the Court of Customs and Patent Appeals, stated that "knowledge of the pharmacological activity of any compound is obviously beneficial to the public" and concluded that "adequate proof of any such utility constitutes a showing of practical utility." *Id.* at 856, 206 U.S.P.Q. (BNA) at 883. n13 The tests n14 found by the court to be adequate proof of pharmacological activity or practical utility were a rat blood pressure (BP) test and a gerbil colon smooth muscle stimulation (GC-SMS) test. The BP test was an *in vivo* test, which was deemed by the court to be direct evidence as to the claimed **[*1047]** activity, while the GC-SMS test was an *in vitro* test. n15

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n13 For purposes of the present opinion, we consider the phrase "substantial utility," as enunciated in *Brenner*, to be synonymous with the phrase "practical utility" as used in subsequent opinions of the CCPA.

n14 We recognize that *Nelson* dealt with tests which were found adequate to establish an actual reduction to practice, as opposed to a constructive reduction to practice. We agree with the Board that principles applicable to a determination of an actual reduction to practice are generally germane to a constructive reduction to practice. **[**20]**

n15 Both parties admitted that the GC-SMS test adequately simulated *in vivo* smooth muscle stimulation.

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The CCPA in *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 1383, 181 U.S.P.Q. (BNA) 453, 454 (1974), stated that HN6 where a count contains no limitation related to utility, evidence establishing a substantial utility for any purpose is sufficient to show a reduction to practice. The court held that three *in vivo* tests n16 conducted in the United States prior to the filing of Englehardt's U.S. application failed to establish an actual reduction to practice. The court proceeded, however, to find sufficient evidence in the record to establish that Englehardt had conceived a utility for his compound prior to the filing date of his U.S. application. The evidence the court found to be sufficient was testimony by the inventor that he believed his compound would exhibit a particular pharmacological activity because of its structural similarity to another

compound which was known to possess the particular pharmacological activity. The court found that the testimonial evidence of Englehardt **[**21]** was corroborated by two exhibits entered into evidence. The evidence adduced by Englehardt was found by the court to be sufficient proof that Englehardt had conceived that his compound had utility for the particular pharmacological activity prior to his U.S. filing date. The court further noted that this was a completed conception of utility because it appeared that nothing beyond the exercise of routine skill would have been required to demonstrate that Englehardt's compound possessed the particular pharmacological utility. While noting that the actual testing done was not sufficient to establish an actual reduction to practice, the court found that the extensive testing done *in vivo* on animals was routine in nature and was not, therefore, to be construed as an indicator that extensive research, i.e., inventive skill and/or undue experimentation, was required to resolve perplexing intricate difficulties related to the utilization of the compound for the particular pharmacological activity.

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n16 The three tests, all *in vivo* type tests carried out on laboratory animals, were: (1) the Mental Health General Screening Test which indicated the physical response, or absence of a response, of test animals to a drug, indicating the presence, or absence, of a desired pharmacological activity; (2) the Tetrabenazine Antagonism Test which screened drugs for antidepressant activity; and (3) the Sidman Avoidance Test which screened drugs for tranquilizing activity.

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The CCPA in *Kawai v. Metlesics*, 480 F.2d 880, 178 U.S.P.Q. (BNA) 158 (1973), concurred with the finding of the Board that the applicants had failed to prove that their foreign priority application was adequate under the patent laws of the United States. The only disclosure in the foreign priority application relating to the compound of the count was that it exhibited "pharmacological effects on the central nervous system," which the applicants conceded was an inadequate disclosure. The applicants, however, relied upon a patent made of record as indicative of the general knowledge of one skilled in the art, which the applicants contended described a compound closely related to their claimed compound, to show utility or pharmacological activity for the compound of the count as an anticonvulsant. The court agreed with the board that there were sufficient structural dissimilarities between the compounds of the patent and those of the count to preclude reliance on the patent to supplement the disclosure deficiencies of the foreign priority application.

In *Knapp v. Anderson*, 477 F.2d 588, 177 U.S.P.Q. (BNA) 688 (CCPA 1973), the court, citing to *Blicke v. Treves*, 44 C.C.P.A. **[**23]** 753, 241 F.2d 718, 112 U.S.P.Q. (BNA) 472 (CCPA 1957), stated that "it is well settled that if the counts do not specify any particular use, evidence proving *substantial utility for any purpose* is sufficient to establish an actual reduction to practice." *Id.* at 590, 177 U.S.P.Q. (BNA) at 690 (emphasis added). Noting that the only utility contemplated for the compounds of the count was as ashless dispersants in lubricant compositions used in internal combustion engines, the court found no error in the Board's holding that there was no actual reduction to practice because **[*1048]** only a potential utility had been established, this holding based upon the Board's finding of a lack of correlation between bench tests and actual service conditions in a combustion engine.

The CCPA has held that nebulous expressions, such as "biological activity" or "biological properties," disclosed in a specification convey little explicit indication regarding the utility of a compound. *In re Kirk*, 54 C.C.P.A. 1119, 376 F.2d 936, 941, 153 U.S.P.Q. (BNA) 48, 52 (CCPA 1967). But, while agreeing with the Board that the specification failed to disclose a specific allegation of utility for **[**24]** any compound within the scope of the claims, and that reference in the specification to biological properties of the claimed compound was so general and vague as to be meaningless, the court implied that a disclosure in the specification that the requisite properties of the claimed compounds are similar to those of a natural or synthetic

hormone of known activity may, in appropriate circumstances, supplement an application to rectify an inadequate disclosure relating to the practical utility for the compound. *Id.* at 942, 153 U.S.P.Q. (BNA) at 53.

HN7 Every utility question arising in an interference, in the final analysis, must be decided on the basis of its own unique factual circumstances. Relevant evidence must be judged as a whole for its persuasiveness in determining whether the suggested use for the compound of the count is a practical utility. *Cf.* Nelson, 626 F.2d at 858, 206 U.S.P.Q. (BNA) at 885.

The Board has found that the Japanese priority application of Iizuka disclosed a practical utility for the compounds of the phantom count in the inhibition of thromboxane synthetase in human or bovine platelet microsomes, i.e., an *in vitro* utility. Clearly, this stated **[**25]** utility as found by the Board has been delimited with sufficient specificity to satisfy the threshold requirements of *Kawai* and *Kirk*. The stated utility of the Japanese priority application is directed to a specific pharmacological activity possessed by the imidazole derivatives of the phantom count -- the inhibition of thromboxane synthetase *in vitro*. Thus, this court on review is not presented with a general allegation of "biological activity" or "biological properties" as was the CCPA in *Kirk*, nor is reliance on prior art required to ascertain what specific pharmacological activity the compound of the count possesses, the factual situation confronting the court in *Kawai*.

The Japanese priority application, moreover, disclosed that it was generally known in the art, as of the critical date, that the parent imidazole and 1-methylimidazole compounds possessed an inhibitory action for thromboxane synthetase. Reliance on this disclosure in the specification of the pharmacological property of the parent imidazole and 1-methylimidazole compounds, as going towards proof of the pharmacological activity of the imidazole derivatives of the phantom count, is particularly **[**26]** relevant in the instant case, we believe, because Iizuka is not relying on this inference to supplement an inadequate disclosure in the Japanese priority application regarding the pharmacological activity of the compound of the phantom count, but rather is relying on this inference as cumulative probative evidence showing an adequately disclosed practical utility in the Japanese priority application.

This court, in *Rey-Bellet* and *Kawai*, has implied that HN8 a particular pharmacological activity identified with prior art compounds may have probative value as to the fact that the compound of the count possesses this particular pharmacological activity where there is a structural similarity between the prior art compounds and the compound of the count. Rey-Bellet, 493 F.2d at 1385-87, 181 U.S.P.Q. (BNA) at 456-58; Kawai, 480 F.2d at 890-91, 178 U.S.P.Q. (BNA) at 166-67. Cross has failed to proffer sufficient evidence or present any persuasive arguments going to the question of significant structural dissimilarities between the parent imidazole and 1-methylimidazole compounds and the imidazole derivatives of the phantom count. n17

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n17 Contrary to Cross' contention in the Reply Brief, the evidence of record relied upon by Cross to show significant structural dissimilarity appears to us to be directed to the fact that there is a wide disparity in potency for thromboxane synthetase inhibition between the parent imidazole compound and prior art imidazole derivatives. Cross has not directed our attention to any specific evidence of record which establishes, or tends to establish, significant structural dissimilarities between the basic imidazole compound and the imidazole derivatives of the phantom count. Variation in potency, moreover, is a matter of degree of activity, *see* Bundy, 642 F.2d at 433, 209 U.S.P.Q. (BNA) at 51, but is still indicative of activity. There is no requirement that the compounds have the same degree of activity. *Id.*, 209 U.S.P.Q. (BNA) at 51. Moreover, this argument may be construed as a tacit admission that the parent imidazole compound does possess the particular pharmacological activity of inhibiting thromboxane synthetase.

Along this line, we note that Dr. Smith, Cross' expert witness, testified generally, based upon

the exhibits proffered by Iizuka, *see infra* note 18, that the parent imidazole compound possessed pharmacological activity for inhibiting thromboxane synthetase, although stating that there was a wide potency spectrum for prior art imidazole derivatives with respect to the parent imidazole compound.

Cross has directed the court's attention to the fact that the Japanese priority application, while disclosing that the parent imidazole and 1-methylimidazole compounds possess an inhibitory action for thromboxane synthetase, further discloses that this inhibitory effect is not satisfactory and that the parent imidazole and 1-methylimidazole compounds have not been put to practical therapeutic use. But a therapeutical utility is not necessarily synonymous to a pharmacological activity. *Cf.* Nelson, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883.

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[*1049] The expert of Iizuka, Dr. Ramwell, testified that, as of the critical date, there was an awareness on the part of those skilled in the art that the parent imidazole compound exhibited an inhibitory activity for thromboxane synthetase, in both *in vitro* and *in vivo* environments. Dr. Ramwell further testified that there was an awareness by those skilled in the art of a correlation between thromboxane A[2] and platelet aggregation, namely that thromboxane A[2] was a mediator in platelet aggregation. Several exhibits proffered by Iizuka corroborated Dr. Ramwell's testimony as to the general knowledge in the art with respect to the inhibitory effect of the parent imidazole compound for thromboxane synthetase. n18 Accordingly, the similar pharmacological activity of the parent imidazole and 1-methylimidazole compounds have probative value in the factual determination of practical utility for the compounds of the phantom count inasmuch as Cross has not met the burden of proof to establish structural dissimilarities between the parent imidazole and 1-methylimidazole compounds and the imidazole derivatives of the phantom count. Rey-Bellet, 493 F.2d at 1386-87, **[**28]** 181 U.S.P.Q. (BNA) at 457.

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n18 For example, Table I in the article "*Imidazole*: A Selective Inhibitor of Thromboxane Synthetase," PROSTAGLANDINS, Vol. 13, No. 4, April 1977 (Iizuka Exhibit No. 6), lists 1-methylimidazole and the parent imidazole compounds as possessing inhibitory activity for thromboxane synthetase, thereby offering corroboration of Dr. Ramwell's testimony.

The Board noted that Iizuka Exhibits 2-6 and 10-12, while inadmissible for the purpose of establishing the truth of what they say on their face, are admissible to bolster and support the testimony of Dr. Ramwell, as well as for the purpose of establishing what literature was available to the art at the critical time. Thus, for review purposes, we have examined these exhibits for their corroborating value with respect to Dr. Ramwell's testimony.

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The Board found that there was adequate proof that the Japanese priority application disclosed a pharmacological activity for the compounds of the phantom count in inhibiting the action of **[**29]** thromboxane synthetase, similar to the pharmacological activity of the parent imidazole and l-methylimidazole compounds which were found to possess an inhibitory action for thromboxane synthetase, this disclosed knowledge of the inhibitory action of the prior art compounds having been corroborated by testimony and documentary evidence. During the proceedings before the Board, the burden of proof rested upon Cross to show that the Japanese priority application was deficient. 37 C.F.R. § 1.257(a). On review, Cross bears the burden of proof to show that the Board erred in finding that the Japanese priority application had adequately disclosed a practical utility. Reviewing the relevant evidence presented to the Board as a whole, we are not persuaded that Cross has met this burden of proof.

[*1050] The final question we must address is whether the inhibitory activity for thromboxane synthetase in human or bovine platelet microsomes, i.e., an *in vitro* utility, is sufficient to comply with the practical utility requirement of § 101. Based upon the facts of this case, we are not persuaded that the Board erred in finding that the *in vitro* utility disclosed in the Japanese **[**30]** priority application for the compounds of the count is sufficient to establish a practical utility.

Our predecessor court has noted that HN9 adequate proof of any pharmacological activity constitutes a showing of practical utility. *See, e.g.,* Nelson, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883; *Rey-Bellet*, 493 F.2d at 1383, 181 U.S.P.Q. (BNA) at 454. Dr. Ramwell testified that initial testing of compounds for a particular pharmacological activity is typically done *in vitro. In vitro* testing permits an investigator to establish the rank order of compounds with respect to the particular pharmacological activity, i.e., to determine the relative potency of the compounds. Compounds having the highest ranking or potency are then selected for further testing *in vivo*. Presumably this is the accepted practice in the pharmaceutical industry inasmuch as Cross has not proffered any evidence refuting this testimony of Dr. Ramwell, and we note that this practice has an inherent logical persuasiveness. *In vitro* testing, in general, is relatively less complex, less time consuming, and less expensive than *in vivo* testing. Moreover, *in vitro* results with respect to the particular **[**31]** pharmacological activity are generally predictive of *in vivo* test results, i.e., there is a reasonable correlation therebetween. Were this not so, the testing procedures of the pharmaceutical industry would not be as they are. Iizuka has not urged, and rightly so, that there is an invariable exact correlation between *in vitro* test results and *in vivo* test results. Rather, Iizuka's position is that successful *in vitro* testing for a particular pharmacological activity establishes a significant probability that *in vivo* testing for this particular pharmacological activity will be successful.

As discussed above, Dr. Ramwell testified that the parent imidazole and 1-methylimidazole compounds had been subjected to both *in vitro* and *in vivo* testing as of the critical date, this corroborated by documentary evidence, and found to possess an inhibitory effect for thromboxane synthetase. Based upon this, Dr. Ramwell further testified that he would expect that *in vivo* testing of the imidazole derivatives of the phantom count would show that these compounds also possessed an inhibitory action for thromboxane synthetase, i.e., there would be a reasonable correlation **[**32]** between *in vitro* test results and *in vivo* test results. This evidence was found sufficient by the Board as proof that the Japanese priority application had disclosed a completed practical utility for the imidazole derivatives of the phantom count in inhibiting thromboxane synthetase in human or bovine platelet microsomes. *Cf.* Rey-Bellet, 493 F.2d at 1386-87, 181 U.S.P.Q. (BNA) at 457.

Cross argues that the *in vitro* utility disclosed by the Japanese priority application is not *per se* useful, and that more sophisticated *in vitro* tests, using intact cells, or *in vivo* tests are necessary to establish a practical utility. n19 Cross is arguing that there must be a rigorous correlation of pharmacological activity between the disclosed *in vitro* utility and an *in vivo* utility to establish a practical utility. We, however, find ourselves in agreement with the Board that, based upon the relevant evidence as a whole, there is a reasonable correlation between the disclosed *in vitro* utility and an *in vivo* activity, and therefore a rigorous correlation is not necessary where the disclosure of pharmacological activity is reasonable based upon the probative **[**33]** evidence. *Cf.* Nelson, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883-83.

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n19 Cross is seemingly arguing that the *in vitro* disclosure of the Japanese priority application is only a *potential* utility. *See* Knapp v. Anderson, 477 F.2d 588, 591, 177 U.S.P.Q. (BNA) 688, 691 (CCPA 1973).

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Our predecessor court has accepted evidence of *in vivo* utility as sufficient to **[*1051]**

establish a practical utility. *See, e.g.,* Nelson v. Bowler, 626 F.2d 853, 206 U.S.P.Q. (BNA) 881 (CCPA 1980); *In re Jolles*, 628 F.2d 1322, 206 U.S.P.Q. (BNA) 885 (CCPA 1980); *Rey-Bellet v. Engelhardt*, 493 F.2d 1380, 181 U.S.P.Q. (BNA) 453 (CCPA 1974).

Opinions of our predecessor court have recognized the fact that pharmacological testing of animals is a screening procedure for testing new drugs for practical utility. *See, e.g., In re Jolles*, 628 F.2d 1322, 1327, 206 U.S.P.Q. (BNA) 885, 890 (CCPA 1980). This *in vivo* testing is but an intermediate link in a screening chain which may eventually lead to **[**34]** the use of the drug as a therapeutic agent in humans. We perceive no insurmountable difficulty, under appropriate circumstances, in finding that the first link in the screening chain, *in vitro* testing, may establish a practical utility for the compound in question. Successful *in vitro* testing will marshal resources and direct the expenditure of effort to further *in vivo* testing of the most potent compounds, thereby providing an immediate benefit to the public, analogous to the benefit provided by the showing of an *in vivo* utility. *Cf.* Nelson, 626 F.2d at 856, 206 U.S.P.Q. (BNA) at 883.

Today, under the circumstances of the instant case, where the Japanese priority application discloses an *in vitro* utility, i.e., the inhibition of thromboxane synthetase in human or bovine platelet microsomes, and where the disclosed *in vitro* utility is supplemented by the similar *in vitro* and *in vivo* pharmacological activity of structurally similar compounds, i.e., the parent imidazole and 1-methylimidazole compounds, we agree with the Board that this *in vitro* utility is sufficient to comply with the practical utility requirement of § 101.

3. Enablement **[**35]**

The Board found that the knowledge as to the use of the pharmacological activity disclosed in the Japanese priority application lay in the fact that the system was a microsome system, microsome systems admittedly being known to those skilled in the art. Employing a microsome assay, the skilled worker could determine the relative strength of the compounds of the count vis-a-vis the known parent imidazole and 1-methylimidazole compounds. Thus, the dosage in the microsome assay milieu could be determined without inventive skill or undue experimentation.

Since we have agreed with the Board that the practical utility for the imidazole derivatives of the phantom count lies in their pharmacological activity in the microsome environment, the how-to-use requirement of § 112 must be analyzed with reference to the microsome environment. We are confronted with a disclosure, similar to the situation before the court in *Bundy*, that fails to reveal dosages for the novel compounds *per se*. 642 F.2d at 434, 209 U.S.P.Q. (BNA) at 51. Although the Japanese priority application does disclose the fact that the imidazole derivatives of the phantom count possess a pharmacological activity **[**36]** similar to the parent imidazole and 1-methylimidazole compounds, the priority application, unlike the application in *Bundy*, does not disclose dosages for the parent imidazole and 1-methylimidazole compounds.

We agree with the Board, however, that this deficiency in the Japanese priority application is not fatal. The testimonial evidence of Dr. Ramwell, corroborated by certain documentary evidence, showed that those skilled in the art had available, at the critical date, information as to approximate dosage levels for the parent imidazole and 1-methylimidazole compounds to produce an I[C50] effect, i.e., a 50% inhibition of thromboxane synthetase, in a microsome milieu. The objective of the pharmaceutical research undertaken by the parties was to discover imidazole derivatives having a potent inhibitory effect for thromboxane synthetase. Therefore, we believe it is logical, as did the Board, that the starting point for determining I[C50] dosage levels for the imidazole derivatives of the phantom count would be the I[C50] dosage levels of the parent imidazole and 1-methylimidazole compounds. The Board found that there was sufficient credible evidence that one skilled **[**37]** in the art, without the exercise of **[*1052]** inventive skill or undue experimentation, could determine the I[C50] dosage level for the imidazole derivatives of the phantom count in the microsome environment. *Cf. Bundy, id.*, 209 U.S.P.Q. (BNA) at 51. We do not believe the Board erred in arriving at this conclusion. This is not a case such as *In re Gardner*, 57 C.C.P.A. 1207, 427 F.2d 786, 166 U.S.P.Q. (BNA) 138

(1970), where the CCPA held that the applicant's disclosure was nonenabling because inventive skill and undue experimentation would be required to discover appropriate dosages for humans, i.e., a therapeutic use. In the instant case, we are confronted with a pharmacological activity or practical utility, not a therapeutic use.

While we agree with the Board that the disclosure in the Japanese priority application is somewhat confusing with respect to the 2.5 x 10<-8> level of molar concentrations, and that the 2-[p-(1-imidazolylmethyl) phenoxy]-acetic acid hydrochloride compound is outside the phantom count of the interference, this disclosed molar concentration, we believe, does provide some probative value going towards the sufficiency of the Japanese priority **[**38]** application for an enabling disclosure. The disclosed molar concentration would provide sufficient information as to an initial dosage level so that one skilled in the art could determine, without inventive skill or undue experimentation, the necessary molar concentrations for the imidazole derivatives of the phantom count to achieve the desired pharmacological effect, i.e., the 50% inhibition of thromboxane synthetase in human or bovine platelet microsomes.

The Board held the disclosure of the Japanese priority application adequate to satisfy the first paragraph of § 112. The burden is on Cross to show Board error in arriving at this conclusion, and we are not persuaded that Cross has successfully carried this burden. Accordingly, we are satisfied that the how-to-use requirement of § 112 has been complied with by the disclosures of the Japanese priority application.

AFFIRMED.

*493 F.2d 1380, *; 1974 CCPA LEXIS 181, **;*
181 U.S.P.Q. (BNA) 453

GERALD REY-BELLET AND HANS SPIEGELBERG, Appellants, v. EDWARD L. ENGELHARDT, Appellee, v. WALTER SCHINDLER, Appellee.

EDWARD L. ENGELHARDT, Appellant, v. GERALD REY-BELLET AND HANS SPIEGELBERG, Appellees, v. WALTER SCHINDLER, Appellee.

Patent Appeal Nos. 8998 and 8999

UNITED STATES COURT OF CUSTOMS AND PATENT APPEALS

493 F.2d 1380; 1974 CCPA LEXIS 181; 181 U.S.P.Q. (BNA) 453

April 4, 1974, Decided.

PRIOR HISTORY: [1]** Interference No. 94,557.

CASE SUMMARY

PROCEDURAL POSTURE: Appellants challenged the decision of the Patent Office Board of Patent Interferences that awarded priority of invention for a chemical compound to appellee in two patent interference actions.

OVERVIEW: In a consolidation of two actions, the Patent Office Board of Patent Interferences (Board) awarded priority of invention for a chemical compound to appellee, concluding that neither appellant had proven their dates of invention earlier than the date of appellee's patent application, March 14, 1961. On appeal, the court reversed the Board's decision with regard to one appellant as he had conceived the invention no later than January of 1961 and was reasonably diligent in a constructive reduction of his invention to practice. Despite only testing the compound on animals before applying for the patent, the court held that the appellant's conception of utility for the compound as an antidepressant was complete because this testing was within the exercise of routine skill required to demonstrate that it had this activity. No consideration of the other appellant's challenge was made as his alleged date of invention was after January of 1961.

OUTCOME: The court reversed the decision awarding priority of invention to appellee because one appellant had conceived his invention prior to the date of appellee's patent application being filed and appellant was reasonably diligent in constructively reducing his invention to practice. Other appellant's challenge was not considered.

CORE TERMS: antidepressant, reduction, invention, animal, compound, amitriptyline, diligence, testing, tranquilizing, conceived, tetrabenazine, monkey, filing date, patent, constructive, accorded, serial, tranquilizer, routine, shock, skill, earliest, screening, similarity, therapy, reasonable diligence, antagonism, anticholinergic, preparation, depression

LexisNexis(R) Headnotes ◆ Hide Headnotes

Patent Law > Utility Requirement > Chemical Compounds
Patent Law > Nonobviousness > Date of Invention
HN1 An actual reduction to practice of an invention can be shown by the establishment of a practical utility. More Like This Headnote

Patent Law > Utility Requirement > Chemical Compounds
Patent Law > Nonobviousness > Date of Invention

HN2 Evidence which would establish a substantial utility of an invention for any purpose is sufficient to show its reduction to practice. More Like This Headnote

Patent Law > Utility Requirement > Chemical Compounds
Patent Law > Nonobviousness > Date of Invention
HN3 There are a number of decisions in which the results of tests done on laboratory animals are considered to be adequate to prove a reduction to practice. These cases fall into two categories. One category includes those cases in which the tests, though carried out on animals, are considered to prove that the drug would be useful in human therapy. This situation arises when there exists a satisfactory correlation between the effect on the animal and that ultimately observed in human beings. The other category is made up of those cases in which the tests done on animals, even though they might have been designed to indicate a utility for human therapy, prove that the drug is useful for treating animals. More Like This Headnote

Patent Law > Nonobviousness > Date of Invention
HN4 Conception of an inventive process involves proof of mental possession of the steps of an operative process and, if necessary, of means to carry it out to such a degree that nothing remains but routine skill for effectuation thereof. If after the claimed conception date extensive research was found necessary before achieving minimum satisfactory performance obviously the mental embodiment of that date was a mere hope or expectation, a statement of a problem, but not an inventive conception. When an invention is followed by extensive research characterized by perplexing intricate difficulties arising every step of the way, then accordingly it is held not to constitute evidence of conception of the invention of the count. More Like This Headnote

Patent Law > Nonobviousness > Date of Invention
HN5 That which determines if the mental formulation of the invention rises to the level of conception is whether or not the inventor has also conceived the means of putting that formulation in the hands of the public where no more than routine skill would be required to do so. More Like This Headnote

Patent Law > Utility Requirement > Chemical Compounds
Patent Law > Nonobviousness > Date of Invention
HN6 The extent of testing or other research done after the mental formulation of an invention is not a reliable indicator that "perplexing intricate difficulties" have been encountered. A more reliable criterion is the nature of this research. More Like This Headnote

Patent Law > Nonobviousness > Date of Invention
HN7 That the activity of those engaged in the preparation of a patent application accrues to the benefit of the inventor for the purpose of showing diligence requires no citation of authority. More Like This Headnote

Patent Law > Nonobviousness > Date of Invention
HN8 Work on related applications can be relied upon to show reasonable diligence. More Like This Headnote

Patent Law > Nonobviousness > Date of Invention
HN9 As long as an inventor is found to be diligent in working actually to reduce his invention to practice, he is not under an obligation to file a patent application. More Like This Headnote

OPINIONBY: BALDWIN

OPINION: [*1381]

BALDWIN, Judge.

These appeals are from the decision of the Patent Office Board of Patent Interferences awarding priority of invention of the sole count in issue to Schindler, the senior party of this three party interference. n1 We reverse the board's decision and hold that priority should have been awarded to the party Engelhardt.

n1 The interference involved in the board's decision is a consolidation of two interferences and originally there were five parties. Two of these suffered adverse decisions in earlier Patent Office proceedings and are no longer parties to the interference.

The Appeals

Schindler is involved in these appeals on application serial No. 282,874, filed May 24, 1963, as a continuation-in-part of application serial No. 179,482, filed March 13, 1962. Schindler claimed and **[*1382]** was accorded the benefit under 35 USC 119 of two Swiss applications. The earliest of these, Swiss No. 3054/61, had a filing date of March 14, 1961. This date became his date of invention for the purpose of the interference contest conducted below.

Appeal No. 8998 is the appeal of the party Rey-Bellet Bellet **[**2]** et al. (Rey-Bellet) involved on application serial No. 463,345, filed June 11, 1965, as a continuation-in-part of application serial No. 170,787, filed February 2, 1962. Rey-bellet claimed and was accorded the benefit of two earlier Swiss applications, the earliest of which, Swiss No. 11,063/61, had a filing date of September 22, 1961. Rey-Bellet also claimed the benefit of an even earlier Swiss application, Swiss No. 1467/61, filed February 8, 1961. However, the board held that this application failed to satisfy the requirements of the first paragraph of 35 USC 112 and could not, therefore, be the basis of a claim for priority purposes made under § 119. Accordingly, Rey-Bellet was restricted to the September 22, 1961, filing date of Swiss No. 11,063/61 for a date of invention.

Appeal No. 8999 is the appeal of the party Engelhardt involved in serial No. 297,710, filed July 25, 1963. Engelhardt was accorded the benefit of an earlier filed U.S. application, serial No. 120,835, filed May 24, 1961, but alleged an even earlier conception and actual reduction to practice. In the alternative, Engelhardt alleged diligence between the conception and the 1961 filing date. However, **[**3]** the board held these allegations not to have been proven and restricted Engelhardt to the May 24, 1961, filing for date of invention.

Having concluded that neither Rey-Bellet nor Engelhardt had proven dates of invention earlier than March 14, 1961, the board awarded priority to Schindler.

The Subject Matter

The sole count of this interference is directed to a chemical compound and reads as follows:

5-(3-methylaminopropylidene) dibenzo-[a, d]-cyclohepta [1, 4] diene.

The parties to these appeals refer to this compound by a less cumbersome name, nortriptyline, which is usually abbreviated to NTL. Nortriptyline (hereinafter NTL) is an anti-depressant compound at moderate levels, but acts as a tranquilizer at high dosage levels. It has the following chemical structure:

[Graphic omitted. See illustration in original.]

OPINION

From the posture of the parties to these appeals, Engelhardt would legally be entitled to priority over Schindler in either of two circumstances. He can prove either that he made an actual reduction to practice of the invention before March 14, 1961, the unchallenged date of invention accorded Schindler by the board, or that he conceived **[**4]** the invention before that date and was diligent from a point in time before that date to a subsequent actual or constructive reduction to practice. In fact, Engelhardt argues that he has satisfied his burden of proof relative to either circumstance, although he principally relies on the allegation that he completed an actual reduction to practice prior to Schindler's date of invention.

The Alleged Actual Reductions to Practice

It is undisputed that the compound corresponding to the count had been prepared in this country by Engelhardt no later than December of 1960, while employed at the Merck, Sharp and Dohme Research Laboratories (Merck). Accordingly, all that remained for HN1 an actual **[*1383]** reduction to practice was the establishment of a practical utility. See, e.g., Anderson v. Natta, 480 F.2d 1392, 178 USPQ 458 (CCPA 1973) and Blicke v. Treves, 44 CCPA 753, 241 F.2d 718, 112 USPQ 472 (1957). Since the count contains no limitation related to any utility, HN2 evidence which would establish a substantial utility for any purpose is sufficient to show its reduction to practice. Campbell v. Wettstein, 476 F.2d 642, 177 USPQ 376 (CCPA 1973).

Engelhardt urges that the satisfaction **[**5]** of these legal tests can be found in the results of each of three tests carried out at Merck on laboratory animals. All of these tests were made at Merck by personnel other than the inventor.

The earliest of these tests, the Mental Health General Screening Test, was accomplished in December of 1960. This test is carried out by administering a candidate drug to mice intraperitoneally at differing dosage levels. This test is not designed to detect any specific property of a drug. Instead a number of physical responses of the test animal to the drug are observed. These responses, and for that matter the absence of a response, can be indicative of the presence or absence of a desirable pharmacological property in the drug. The test also gives an indication of the toxicity of the drug.

The second of these tests is known at Merck as the Tetrabenazine Antagonism Test. Again, the test animals are mice. In this test the candidate drug is first administered to the animal followed by a later administration of tetrabenazine. Tetrabenazine is a tranquilizer.

The purpose of the test is to screen candidate drugs for antidepressant activity. The detection of antidepressant activity **[**6]** in a drug using test animals is particularly difficult since the animal is not depressed. The role of tetrabenazine is to chemically simulate depression in the mouse through its tranquilizing effect. To the extent that the candidate drug offsets the tranquilizing effect of tetrabenazine it is said to be an "antagonist" of this effect. Typically a successful test is indicated when the test animal remains active after the sequential administration of the "antagonist" and tetrabenazine. NTL was screened using this test on March 10 and March 29, 1961.

At the time this test was used on NTL at Merck, it was newly developed. However, a similar test using a different drug to simulate depression was under investigation at the National Institutes of Health.

The third test, a so called Sidman Avoidance Test, was made on March 14, 1961. The purpose of this test is to screen drugs for tranquilizing activity. The test animals are squirrel monkeys. The test is carried out by placing the monkey in a cage having a grid floor which is wired to produce a shock every eight seconds. The monkey is trained to avoid shock by pressing a lever which delays the shock for 48 seconds. The average **[**7]** monkey has a high rate of avoidance of shock. However, if the monkey is tranquilized he becomes indifferent to the consequences of being shocked and more likely to fail to press the lever. Therefore, the

potential effect of a drug as a tranquilizer is measured by the performance of a test animal in avoiding shock before and after administration of the drug.

Despite positive indications from these tests that NTL possesses pharmacological activity, the board was of the opinion that the results of the tests did not establish a reduction to practice for the reason that they failed to prove that the compound had any particular utility. Specifically, the board felt that the tests did not demonstrate that NTL would exhibit antidepressant or tranquilizing activity in man. As additional support for its holding that the tests were not adequate to prove a reduction to practice, the board concluded that the record did not reveal any conviction of success at Merck regarding the outcome of these tests being sufficient to show that NTL would be an antidepressant or tranquilizer. **[*1384]**

In his attempt to show error in the board's decision, Engelhardt has directed our attention to HN3 a **[**8]** number of decisions of this court in which the results of tests done on laboratory animals were considered to be adequate to prove a reduction to practice. We view these cases as falling into two categories.

One category includes those cases in which the tests, though carried out on animals, were considered to prove that the drug would be useful in human therapy. This situation arises when there exists a satisfactory correlation between the effect on the animal and that ultimately observed in human beings. See, e.g., Engelhardt v. Judd, 54 CCPA 865, 360 F.2d 408, 151 USPQ 732 (1966).

The other category is made up of those cases in which the tests done on animals, even though they might have been designed to indicate a utility for human therapy, prove that the drug is useful for treating animals. See, e.g., Campbell v. Wettstein, supra; Blicke v. Treves, supra; In re Hitchings, 52 CCPA 1141, 342 F.2d 80, 144 USPQ 637 (1965); In re Krimmel, 48 CCPA 1116, 292 F.2d 948, 130 USPQ 215 (1961); and Archer v. Papa, 46 CCPA 835, 265 F.2d 954, 121 USPQ 413 (1957).

We have considered the character of Engelhardt's evidence as it is embodied in the three tests described above. In our **[**9]** view it fails to establish a reduction to practice within either category of cases for reasons set forth more fully below.

Engelhardt considers the Mental Health General Screening Test as adequate to prove a reduction to practice in two ways. One allegation made is that this test proves NTL has anticholinergic activity because its administration caused the pupils of the eyes of the test animals to dilate.However, the record simply does not support this contention. One of his own witnesses testified that drugs other than those having anticholinergic activity can cause pupil dilation. Therefore, the test cannot be regarded as being specific for this property.

Another allegation made by Engelhardt is based on the structural similarity between NTL and a drug known as amitriptyline, n2 known to be an antidepressant when NTL was made. According to the testimony of one of Engelhardt's witnesses, the results on the screening test for these two drugs were similar. However, it seems clear from the record that this test is unsuited for detecting antidepressant, tranquilizing and anticholinergic activity, the only useful properties possessed by amitriptyline. Therefore, we cannot conclude **[**10]** that the similarity between the two in the screening test is adequate to prove that NTL has any of the aforementioned properties.

n2 Amitriptyline has the following formula:

[Graphic omitted. See illustration in original.]

It differs from NTL by having two CH(3)-substitutes on the nitrogen atom (N) rather than one. Amitriptyline has slight tranquilizing and anticholinergic activity.

The results of the tetrabenazine antagonism test are also inadequate to prove a reduction to practice as an antidepressant. As indicated above, the test was newly developed in 1961. Therefore, the test cannot be regarded as having been an adequate predictor of antidepressant activity in human beings because at the time the test was run there was insufficient experience with it to show the necessary correlation between tetrabenazine antagonism in mice and antidepressant activity in man.

The tetrabenazine antagonism test also fails as an indicator that NTL would be useful in animal therapy.In the first place it has not been established that the property of tetrabenazine **[*1385]** antagonism is per se useful. Secondly, the record established that mice are not depressed, hence the **[**11]** need for chemical simulation of depression using a tranquilizer. Therefore, NTL cannot be regarded as being useful for alleviating depression in animals.

We have also concluded that the Sidman Avoidance Tests run with NTL fail to prove a substantial utility for the drug as a tranquilizer. From the record it appears that NTL demonstrated only weak tranquilizing activity in squirrel monkeys as indicated by their reduced ability to avoid shock. In our view, such a poor showing by NTL in this test cannot be regarded as proof that tranquilizing activity would be observed in man.

We also note that the record reveals that very large doses of NTL were required to cause the tranquilizing effect in monkeys. This makes the results suspect if for no other reason than it suggests correspondingly large doses would be required to affect a human subject if any effect at all could be observed. At such doses the possibility that harmful side effects would occur, which would negate any tranquilizing properties, becomes very much enhanced.

With regard to animal therapy, we need only observe that the record is devoid of any indication that the ability to tranquilize monkeys, particularly **[**12]** the very slight ability shown for NTL, is a property having substantial utility.

The Alleged Conception

In the board's opinion, Engelhardt failed to prove that he had conceived the invention prior to May 24, 1961, the filing date of the U.S. patent application, the benefit of which was accorded Engelhardt for priority purposes. The board felt this was justified notwithstanding the fact that Engelhardt had actually made the compound in this country no later than December of 1960. In its view, Engelhardt failed because he had not proven that he had conceived a particular utility for NTL or the means by which one skilled in the art could reduce to practice this utility without exercising more than routine skill.

In the board's view then, even when the invention is a chemical compound which has been made and is defined by a count reciting no limitation related to its use, conception of that invention is not complete absent a conception of its utility. Engelhardt does not challenge this interpretation of the law. Accordingly, we will treat it as the law of this case although in our minds its applicability remains very much an open question. However, any resolution of this issue **[**13]** should be deferred until squarely presented and briefed by the parties to an appeal.

On the basis of the evidence in the record, we are persuaded that Engelhardt conceived that NTL could be useful as an antidepressant no later than January of 1961. Furthermore, we also believe that no more than routine skill in the art was necessary to reduce this utility to practice.

In its opinion, the board acknowledged Engelhardt's testimony to the effect that he had conceived that NTL would be useful as an antidepressant but dismissed it as lacking corroboration. It also rejected several documentary exhibits as failing to establish conception of this utility. Engelhardt argues that if individually these documents and other evidentiary elements of his case do not establish that he conceived a utility, then collectively they do. We agree.

The gist of the testimony given by Engelhardt is that he felt NTL would have antidepressant activity because of its structural similarity to amitriptyline.It is pointed out above that amitriptyline was known to possess antidepressant activity at the time of the alleged conception by Engelhardt. This testimony, if corroborated, would establish conception **[**14]** by him that NTL could be used as an antidepressant.

The earliest exhibit pertinent to the question of Engelhardt's conception is **[*1386]** Exhibit 9, entitled "Delivery Sheet" and dated December 14, 1960. It is a printed form which, in effect, is a request that tests be conducted on a given compound. Exhibit 9 sets forth the structure of NTL and contains the following notations:

Dr. Stone for screening in the mental health program.

Dr. Hanson for behavioral testing in comparison with "Elavil".

It is pertinent to note that "Elavil" is Merck's trademark for amitriptyline.

The board felt that Exhibit 9 failed as a conception because it did not specifically mention antidepressant activity and for the further reason that:

In our opinion, this falls short of being evidence of conception for the reason that the above instructions to Dr. Stone and Dr. Hanson do not furnish the means to enable one skilled in the art to use the compound for a particular purpose so that nothing remains but routine skill for effectuation of said use.

Another exhibit relied upon by Engelhardt, Exhibit 106, is a handwritten sheet entitled "Compounds for 'Elavil' Program-Clinical." Sixteen **[**15]** compounds were included in the list. All but NTL have been blocked out. That list was read by Dr. James Sprague, Director of Medicinal Chemistry at Merck. In his own hand he added, among other things, the following notation dated January 14, 1961, to the structure of NTL:

Cf. MAO-I + Tofranil

In his brief, Engelhardt alleges that MAO-I stands for monoamine oxidose inhibitors also known to be antidepressants. However, that is not clearly established in the record and we will disregard it. Nevertheless, the record does reveal that "Tofranil" was a well known antidepressant at the time of Engelhardt's alleged conception.

We view these two exhibits as corroborating that Engelhardt had conceived that NTL would have antidepressant activity because of its similarity to amitriptyline. The most significant property of amitriptyline was its antidepressant activity. Structurally it is very similar to NTL and the profiles of the two compounds in the Mental Health Screening Test were very similar. Furthermore, the record does not reveal any other substantial property other than antidepressant activity for which one would seek to compare NTL to amitriptyline.

The testimony of Dr. **[**16]** V. G. Vernier, a supervisor at Merck for the drug screening program, supports this conclusion. He testified that he and Dr. Engelhardt discussed the potential of NTL after he (Dr. Vernier) received Exhibit 9 in December of 1960. He recalled that Engelhardt indicated to him that he expected NTL to have antidepressant activity because of its similarity to amitriptyline.

Schindler, citing Alpert v. Slatin, 49 CCPA 1343, 305 F.2d 891, 134 USPQ 296 (1962), a case also relied upon by the board, argues that these exhibits and this testimony indicate at most a hope that NTL would possess antidepressant activity and as such falls short of being an inventive conception. In Alpert, this court adopted a portion of the board's opinion as its own. A pertinent extract from that portion reads as follows:

HN4 Conception of an inventive process involves proof of mental possession of the steps of an operative process and, if necessary, of means to carry it out to such a degree that nothing

remains but routine skill for effectuation thereof. If after the claimed conception date extensive research was found necessary before achieving minimum satisfactory performance obviously the mental embodiment **[**17]** of that date was a mere hope or expectation, a statement of a problem, but not an inventive conception. Alpert Exh. 4 was followed by extensive research characterized by perplexing intricate difficulties arising every step of the way and accordingly Alpert Exh. 4 is held not to constitute evidence of conception **[*1387]** of the invention of the count. [Emphasis added.]

HN5 That which determines if the mental formulation of the invention rises to the level of conception is whether or not the inventor has also conceived the means of putting that formulation in the hands of the public where no more than routine skill would be required to do so. In this case we think the proof that Engelhardt had conceived of NTL as an antidepressant is sufficient to complete the conception of utility because it appears that nothing beyond the exercise of routine skill would have been required to demonstrate that it had this activity.It is true that extensive testing on animals was done at Merck and that actual clinical trials on humans were not conducted until after the filing date of Engelhardt's parent application. HN6 However, the extent of testing or other research done after the mental formulation **[**18]** of an invention is not a reliable indicator that the "perplexing intricate difficulties" referred to in Alpert have been encountered. A more reliable criterion is the nature of this research.

In this case the record establishes that the tests done at Merck on NTL using test animals were those routinely done to a drug before it is administered to humans. No "perplexing intricate difficulties" had to be overcome. Probably such preliminary testing could have been eliminated in favor of direct testing on humans which would have quickly established whether NTL was an antidepressant. However, the unpredictable response that a human subject might exhibit dictates that considerable preliminary testing in animals be done in order that as much information as possible be known about a drug before it is tested in man. Although in this case the testing done was not sufficient to establish an actual reduction to practice, the policy of conducting such testing is to be applauded rather than penalized.

The Alleged Diligence to a Constructive Reduction to Practice

The adequacy of Engelhardt's parent application as a constructive reduction to practice is not challenged. Therefore, there **[**19]** remains for consideration but one question in Engelhardt's case, that being whether there was diligence from a time before the dates of invention alleged by or accorded to his opponents to the filing date of his parent application. On this point, the board declined to consider whether there was diligence up to March 29, 1961, the date of the last test relied upon by Engelhardt to establish an actual reduction to practice.

The board did hold that there was no evidence of activity between April 21, 1961, the date of an exhibit reporting the results of a Tetrabenazine Antagonism Test, and May 12, 1961, the date of the first draft of the parent application. We believe the record supports the conclusion that there was reasonable diligence during the contested period.HN7

That the activity of those engaged in the preparation of a patent application accrues to the benefit of the inventor for the purpose of showing diligence requires no citation of authority. The responsibility for drafting Engelhardt's application fell to an attorney, Mr. Underwood, in Merck's patent department. He informally requested that Dr. Frank A. Cutler, technical advisor to the patent department, assist him **[**20]** in the preparation of this application. It was Dr. Cutler who prepared the preliminary draft of May 12, 1961. n3

n3 The record indicates that Dr. Cutler prepared two drafts. The second of these was completed on May 15, 1961. Apparently neither could be regarded as a draft of a complete application. Instead they appear to have been descriptions of experimental work appearing in the disclosure of invention. The rest of the specification was prepared by Mr. Underwood.

Dr. Cutler was given on, or shortly after, April 24, 1961, a number of documents **[*1388]** containing descriptions of experiments which he was ultimately to incorporate in the draft of Engelhardt's application. Dr. Cutler testified that he was putting the finishing touches on that draft on May 12, 1961, and would have been working on it before then. This is supported by the fact that several of the documents used by him in preparing the draft contain notations in his own hand.

During the contested time period, it appears that Dr. Cutler, in addition to other duties, was also working on at least one other patent application related to that relied upon by Engelhardt for priority purposes. This application **[**21]** was directed to a process for preparing amitriptyline and closely related compounds including NTL. He testified that he worked on this application concurrently with Engelhardt's application because both were similar in scope and required the same starting materials.The record establishes that Dr. Cutler was working on the process application at least as late as Paril 27, 1961. HN8 Work on related applications can be relied upon to show reasonable diligence. Rines v. Morgan, 45 CCPA 743, 250 F.2d 365, 116 USPQ 145 (1957).

In view of Cutler's activity on the related process case and his testimony that he was working on the draft of Engelhardt's application prior to May 12, 1961, it is our view that there was reasonable diligence during the contest period, a time span of but 21 days.

As we noted above, the board declined to consider whether there was diligence during the period before March 29, 1961. For this time period, both Schindler and Rey-Bellet argue that the only activity which should accrue to Engelhardt's benefit for the purpose of showing diligence running to a constructive reduction to practice is activity directly related to preparing and filing the patent application **[**22]** involved here. Under their view, none of the tests should be considered relevant to whether there was diligence, since all that was required after conception to complete the constructive reduction to practice was preparation and filing of the application.

The view urged upon us by Schindler and Rey-Bellet was rejected by this court in Keizer v. Bradley, 47 CCPA 709, 270 F.2d 396, 123 USPQ 215 (1959). Bradley had been awarded priority based on prior conception and diligence to a constructive reduction to practice. On appeal, Keizer argued that engineering activity directed to an actual reduction to practice could not excuse a lack of "attorney diligence" in preparation of the parent application. On this point, at 47 CCPA 714, 270 F.2d 400, 123 USPQ 218, the court observed:

HN9 As long as Bradley was, as we have found, diligent in working actually to reduce his invention to practice, he was not under an obligation to file a patent application. The fact that he decided to do so does not change the situation.

The arguments of Schindler and Rey-Bellet have not persuaded us that our earlier decision should be reversed. Accordingly, we will consider all of Engelhardt's activities **[**23]** directed to an actual reduction to practice in order to determine if there was diligence. We think the record establishes that there was reasonable diligence from conception to the constructive reduction to practice.

Engelhardt was a chemist whose major responsibility was the synthesis of compounds which were regarded as being of potential interest to Merck. The responsibility for testing these compounds in order to determine whether they had pharmacological activity fell to other persons. The record establishes that Engelhardt requested in December of 1960 that behavioral testing be done for NTL. Such testing would include the Sidman Avoidance Test, but not the Tetrabenazine Antagonism Test which had not been developed at that time. The actual screening of NTL in the Sidman **[*1389]** Avoidance Test did not occur until March 14, 1961. However, the record does not suggest that this was an extraordinary delay.

It appears that Merck's success with amitriptyline and other drugs which affect the central nervous system led to a program in which literally hundreds of compounds were being

screened. As a part of this program, the Sidman Avoidance Test had begun to be used in late **[**24]** 1960 and was available when Engelhardt made his request.

Dr. H. M. Hanson, a pharmacologist at Merck, who was in charge of the Sidman Avoidance Test program, testified on cross-examination that they had but limited facilities in 1961 because of a shortage of monkeys and a limited ability to house them. As a result of this, the test was not often performed.

In the meantime, Dr. Vernier had developed the Tetrabenazine Antagonism Test during February 1961. As soon as Dr. Engelhardt heard of this test, he requested that NTL be employed in it. As we noted supra, this was done on March 10, 1961, and this test gave results which were better than those exhibited by amitriptyline. This test was followed on March 14, 1961, by the Sidman Avoidance Test and on March 29, 1961 by a follow up Tetrabenazine Antagonism Test.

We think this activity establishes that Engelhardt was energetically striving to reduce his invention to practice and was reasonably diligent in this pursuit.

Inasmuch as we hold that Engelhardt conceived the invention no later than January of 1961 and was diligent to a constructive reduction to practice, we need not further consider the appeal of Rey-Bellet, as **[**25]** the earliest date of invention alleged by him is February 8, 1961.

For the foregoing reasons, the board should have awarded priority of invention to Engelhardt. Accordingly, the decision of the board awarding priority of invention to Schindler is reversed.

REVERSED